Ain Shams University
Pediatric Hospital

Pediatric ICU

PICU Protocols

Volume (1)

Pediatric Resuscitation

This section will include:

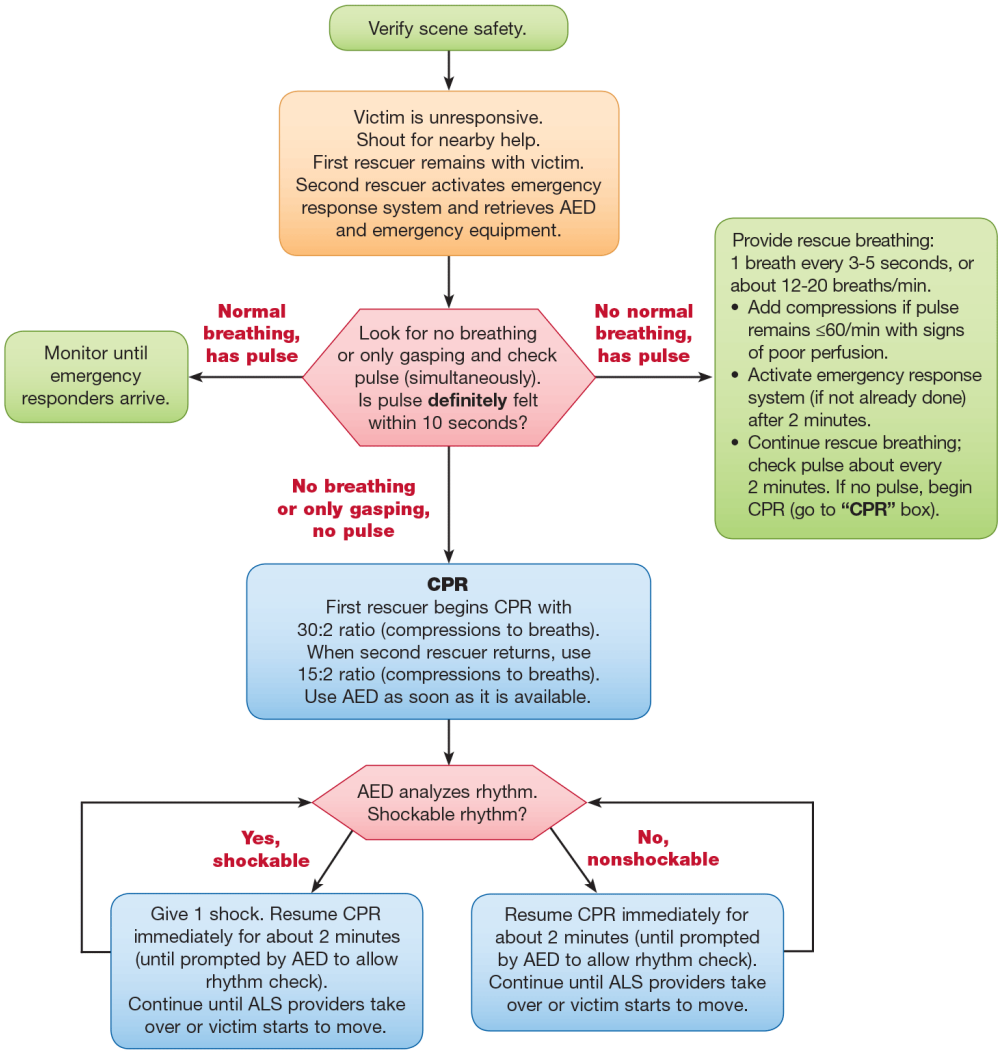
1- Basic life support

2- Advanced life support

3- Post resuscitation care

Basic life support

BLS Healthcare Provider
Pediatric Cardiac Arrest Algorithm for 2 or More Rescuers—2015 Update



1- Assess the Need for CPR: *If the victim is unresponsive and is not breathing (or only gasping), send someone to activate the emergency response system.*

2- Pulse Check: *healthcare providers may take up to 10 seconds to attempt to feel for a pulse (brachial in an infant and carotid or femoral in a child).*

3- Inadequate Breathing with Pulse: *If there is a palpable pulse above 60 per minute but there is inadequate breathing, give rescue breaths at a rate of about 12 to 20 breaths per minute (1 breath every 3 to 5 seconds) until spontaneous breathing resumes.*

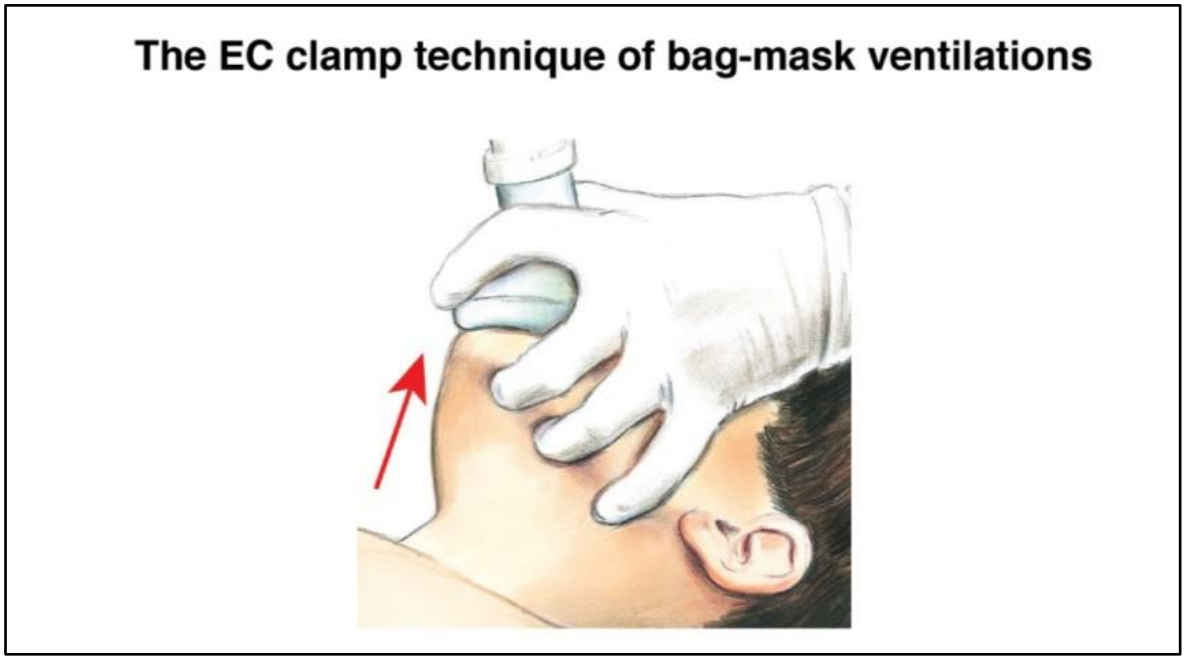
4-Bradycardia with Poor Perfusion: *If the pulse is <60 per minute and there are signs of poor perfusion (ie, pallor, mottling, cyanosis) despite support of oxygenation and ventilation, begin chest compressions.*

5-Chest Compression:

- *Rate: 100 to 120/min.*
- *Depth: depress the chest at least one third the anteroposterior diameter of the chest in pediatric patients.*
  Infants: 1.5 inches (4 cm)
  Children: 2 inches (5 cm)
  Adolescents: 2.4 inches (6 cm)
- *Finger and Hand Placement:*
  For infant, lone rescuers: 2 fingers placed just below the intermammary line.
  2 rescuers: 2thumb–encircling hands technique.
- *Chest Recoil: Allow complete chest recoil after each compression to allow the heart to refill with blood.*
- *Minimizing Interruptions of chest compressions.*

6- Ventilations:

- *After 30 compressions (15 compressions if 2 rescuers), open the airway with a head tilt–chin lift and give 2 breaths*
- *Bag-mask ventilation is an essential CPR technique for healthcare providers*
- *Effective bag-mask ventilation requires a tight seal between the mask and the victim's face. Open the airway by lifting the jaw toward the mask making a tight seal and squeeze the bag until the chest rises*
- *Three fingers of one hand lift the jaw (they form the "E") while the thumb and index finger holds the mask to the face (making a "C").*
- *Cricoid pressure may be considered to decrease gastric inflation which may interfere with effective ventilation and cause regurgitation.*



8- Coordinate Chest Compressions and Ventilations

- *A lone rescuer: 30:2.*
- *For 2-rescuer: 15:2.*

9-The 5 components of high-quality CPR are

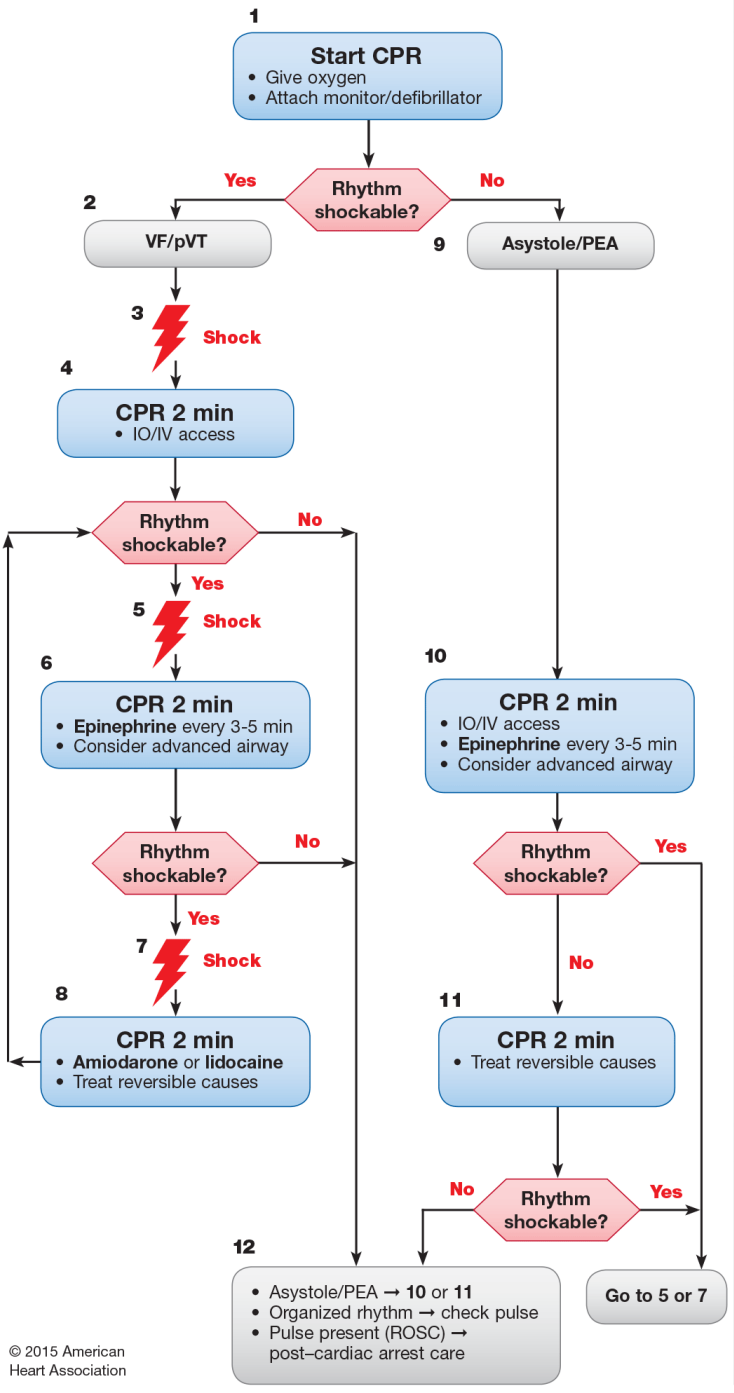
- Ensuring chest compressions of adequate rate
- Ensuring chest compressions of adequate depth
- Allowing full chest recoil between compressions
- Minimizing interruptions in chest compressions
- Avoiding excessive ventilation:

Excessive ventilation is harmful because it

- *Increases intrathoracic pressure and impedes venous return and therefore decreases cardiac output, cerebral blood flow, and coronary perfusion.*
- *Causes air trapping and barotrauma in patients with small-airway obstruction.*
- *Increases the risk of regurgitation and aspiration in patients without an advanced airway.*

Pediatric Advanced Life Support

Pediatric Cardiac Arrest Algorithm—2015 Update



CPR Quality

- Push hard (≥⅓ of anteroposterior diameter of chest) and fast (100-120/min) and allow complete chest recoil.
- Minimize interruptions in compressions.
- Avoid excessive ventilation.
- Rotate compressor every 2 minutes, or sooner if fatigued.
- If no advanced airway, 15:2 compression-ventilation ratio.

Shock Energy for Defibrillation

First shock 2 J/kg, second shock 4 J/kg, subsequent shocks ≥4 J/kg, maximum 10 J/kg or adult dose

Drug Therapy

- **Epinephrine IO/IV dose:** 0.01 mg/kg (0.1 mL/kg of 1:10 000 concentration). Repeat every 3-5 minutes.
  If no IO/IV access, may give endotracheal dose: 0.1 mg/kg (0.1 mL/kg of 1:1000 concentration).
- **Amiodarone IO/IV dose:** 5 mg/kg bolus during cardiac arrest. May repeat up to 2 times for refractory VF/pulseless VT.
- **Lidocaine IO/IV dose:** Initial: 1 mg/kg loading dose. Maintenance: 20-50 mcg/kg per minute infusion (repeat bolus dose if infusion initiated >15 minutes after initial bolus therapy).

Advanced Airway

- Endotracheal intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm and monitor ET tube placement
- Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions

Return of Spontaneous Circulation (ROSC)

- Pulse and blood pressure
- Spontaneous arterial pressure waves with intra-arterial monitoring

Reversible Causes

- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypoglycemia
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

Medications for Pediatric Resuscitation *(American heart association 2015)*		
Medication	**Dose**	**Remarks**
Adenosine	0.1 mg/kg (maximum 6 mg) Second dose: 0.2 mg/kg (maximum 12 mg)	Monitor ECG Rapid IV/IO bolus with flush
Amiodarone	5 mg/kg IV/IO; may repeat twice up to 15 mg/kg Maximum single dose 300 mg	Monitor ECG and blood pressure; adjust administration rate to urgency (IV push during cardiac arrest, more slowly–over 20–60 minutes with perfusing rhythm). Expert consultation strongly recommended prior to use when patient has a perfusing rhythm Use caution when administering with other drugs that prolong QT (obtain expert consultation)
Atropine	0.02 mg/kg IV/IO 0.04–0.06 mg/kg ET* Repeat once if needed Maximum single dose: 0.5 mg	Higher doses may be used with organophosphate poisoning
Calcium Chloride (10%)	20 mg/kg IV/IO (0.2 mL/kg) Maximum single dose 2 g	Administer slowly
Epinephrine	0.01 mg/kg (0.1 mL/kg 1:10 000) IV/IO 0.1 mg/kg (0.1 mL/kg 1:1000) ET* Maximum dose 1 mg IV/IO; 2.5 mg ET	May repeat every 3–5 minutes
Glucose	0.5–1 g/kg IV/IO	Newborn: 5–10 mL/kg $D_{10}W$ Infants and Children: 2–4 mL/kg $D_{25}W$ Adolescents: 1–2 mL/kg $D_{50}W$
Lidocaine	Bolus: 1 mg/kg IV/IO Infusion: 20–50 mcg/kg/minute	
Magnesium Sulfate	25–50 mg/kg IV/IO over 10–20 minutes, faster in torsades de pointes Maximum dose 2 g	
Naloxone	Full Reversal: <5 y or ≤20 kg: 0.1 mg/kg	Use lower doses to reverse respiratory depression associated with therapeutic opioid use (1–5 mcg/kg titrate

Medications for Pediatric Resuscitation *(American heart association 2015)*		
Medication	**Dose**	**Remarks**
	IV/IO/ET* ≥5y or >20 kg: 2 mg IV/IO/ET*	to effect)
Procainamide	15 mg/kg IV/IO Adult Dose: 20 mg/min IV infusion to total maximum dose of 17 mg/kg	Monitor ECG and blood pressure; Give slowly–over 30–60 minutes. Use caution when administering with other drugs that prolong QT (obtain expert consultation)
Sodium bicarbonate	1 mEq/kg per dose IV/IO slowly	After adequate ventilation *Excessive sodium bicarbonate may impair tissue oxygen delivery; cause hypokalemia, hypocalcemia, hypernatremia, and hyperosmolarity decrease the VF threshold and impair cardiac function*

General recommendation for cuffed and uncuffed tracheal tube sizes (internal diameter in mm).

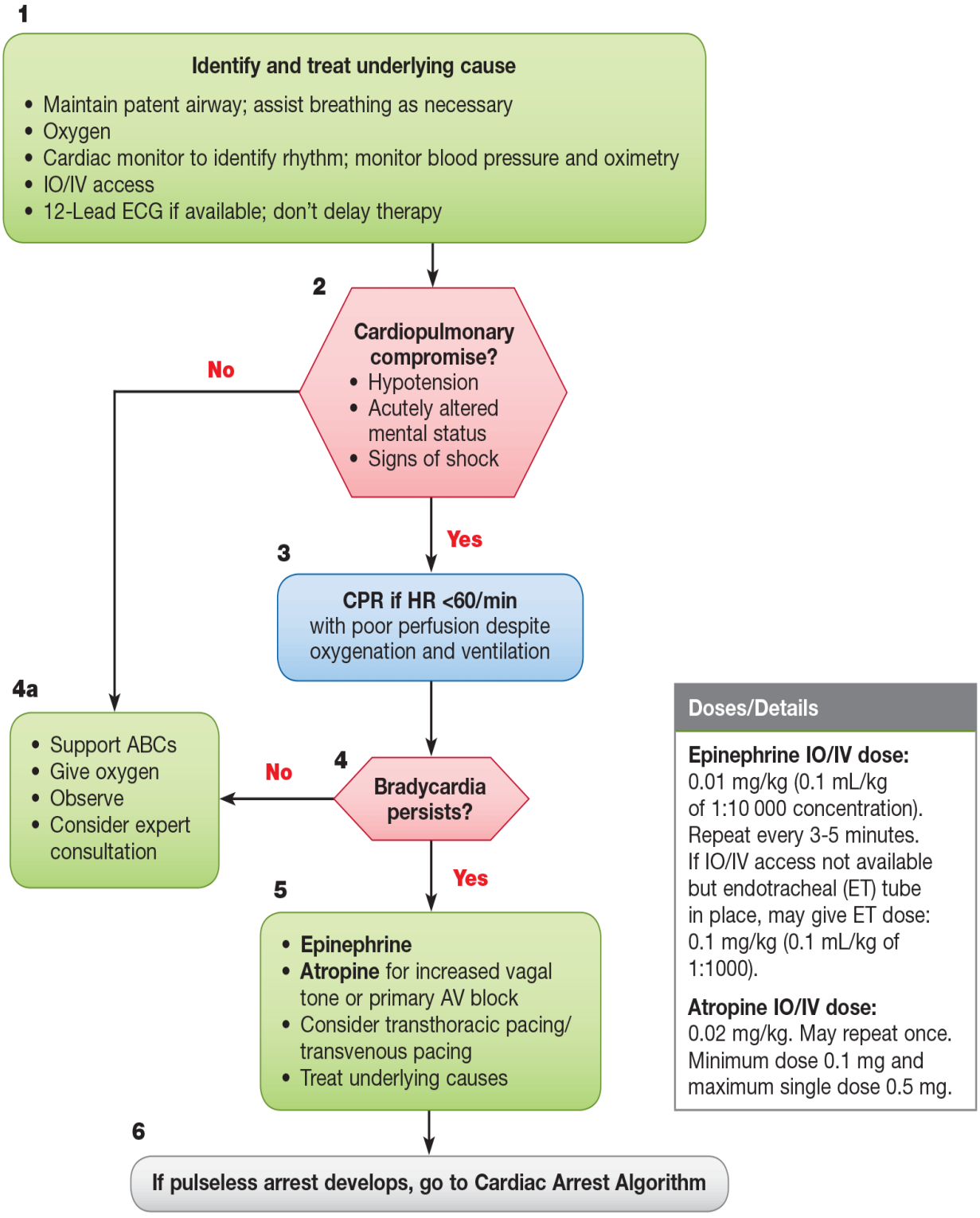
	Uncuffed	Cuffed
Premature neonates	Gestational age in weeks/10	Not used
Full term neonates	3.5	Not usually used
Infants	3.5–4.0	3.0–3.5
Child 1–2 y	4.0–4.5	3.5–4.0
Child >2 y	Age/4 + 4	Age/4 + 3.5

European resuscitation council 2015

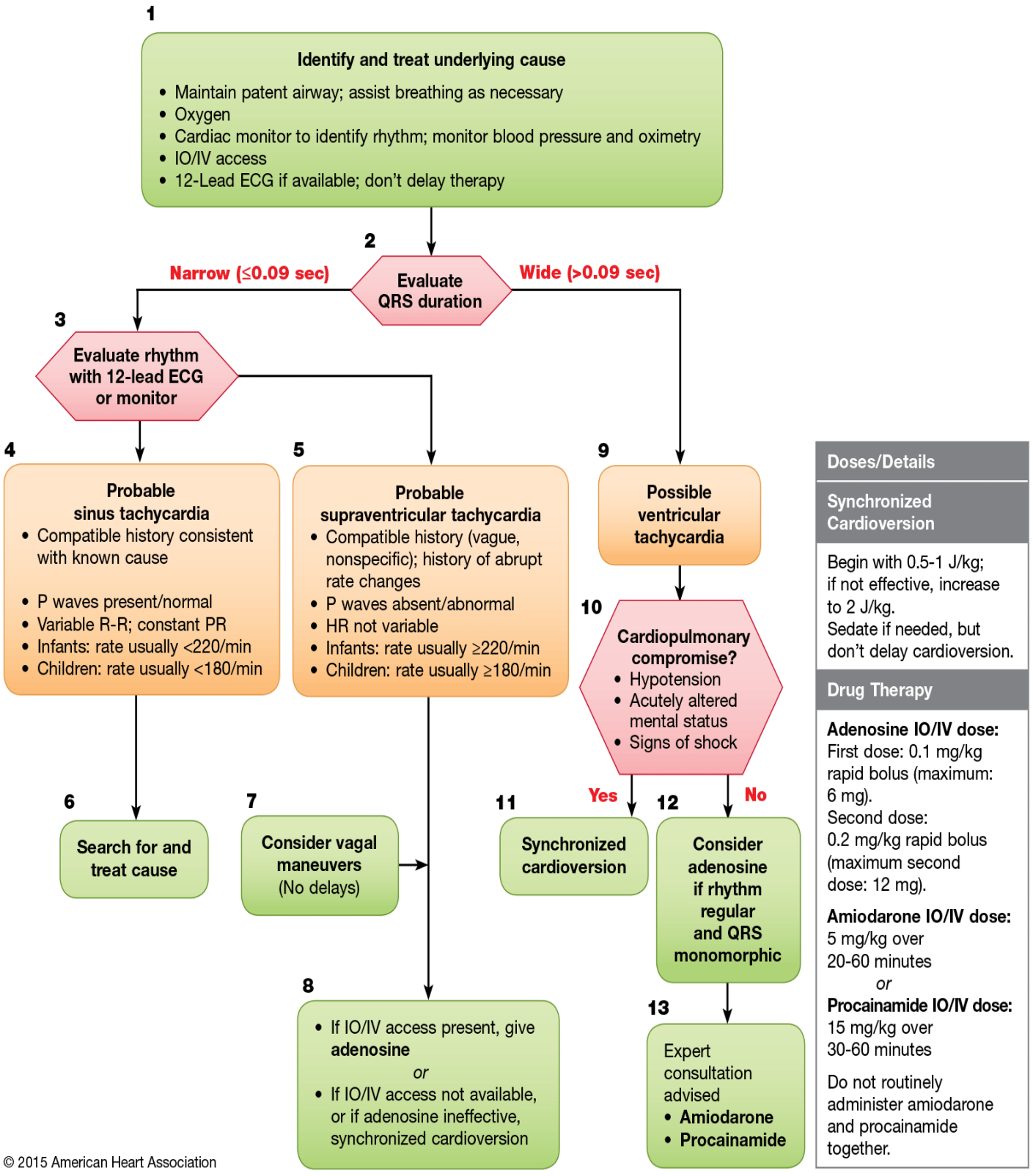
Table (1): Benefits/Risks of intubation methodology

Method of Intubation	Benefits/Risks	Contraindications
Nasotracheal	Benefits	Nasal polyps
	Minimal need for sedation	Coagulation disorder
	Rapidity of preparation	Thrombocytopenia
	Greater postintubation comfort for awake patient	Abnormal nasal anatomy
	Maintenance of semiupright posture	
	Maintenance of spontaneous respiration	
	Decreased likelihood of aspiration	
	Risks	
	Epistaxis	
	Purulent sinusitis	
Orotracheal	Benefits	
	Larger-sized endotracheal tube	
	Direct visualization	
	Relative ease of obtaining pharyngeal anesthesia	
	Risks	
	Oral or tracheal trauma	
	Esophageal intubation	
	Vocal cord injury	
	Aspiration	
Awake orotracheal	Benefits	
	Avoid rendering patient apneic	
	Risks	
	Oral or tracheal trauma	
	Esophageal intubation	
	Vocal cord injury	
	Aspiration	
	Patient might be unable to tolerate the procedure	
	Coughing reflex can be triggered	
Orotracheal with sedation	Benefits	
	Rapid procedure, less traumatic than awake	
	Intubation might be easier to accomplish	
	Risks	
	Oral or tracheal trauma	
	Esophageal intubation	
	Vocal cord injury	
	Aspirationtrun -1	
	Hypotension caused by excessive sedation	
	Opioids might cause bronchospasm	
Orotracheal with neuromuscular blockade	Benefits	
	Increases the ease of intubation by reducing muscular resistance	
	Eliminates the risk of coughing	
	Might provide superior control during intubation compared with sedation alone (Baumgarten, *Can J Anaesth* 1988;35:5–11)	
	Risks	
	Few, rarely serious	
	Side effects of neuromuscular blocking agents	
	Sedation is necessary in addition to neuromuscular blockade	
	Airway loss caused by inability to intubate, ventilate, or both	

Pediatric Bradycardia With a Pulse and Poor Perfusion Algorithm



Pediatric Tachycardia With a Pulse and Poor Perfusion Algorithm



Postarrest Care

The goals of postresuscitation care are to preserve neurologic function, prevent secondary organ injury, diagnose and treat the cause of illness

1-Respiratory System

- maintain normoxemia after ROSC i.e to keep oxygen saturation 94% or above
- target a Paco2 after ROSC that is appropriate to the specific patient condition, and limit exposure to severe hypercapnia or hypocapnia

2- Post–Cardiac Arrest Fluids and Inotropes

After ROSC, parenteral fluids and/or inotropes or vasoactive drugs recommended to be used to maintain a systolic blood pressure greater than fifth percentile for age

Table (2): Normal vital signs according to age *(nelson 20th edition)*

Age	Heart rate (bpm)	Blood pressure	Respiratory rate
Premature	120-170	55-75/35-45	40-70
0-3 mo	100-150	65-85/45-55	35-55
3-6 mo	90-120	70-90/50-65	30-45
6-12 mo	80-120	80-100/55-65	25-40
1-3 yrs	70-110	90-105/55-70	20-30
3-6 yrs	65-110	95-110/60-75	20-25
6-12 yrs	60-95	100-120/60-75	14-22
12 + yrs	55-85	110-130/65-85	12-18

Medications to Maintain Cardiac Output and for Postresuscitation Stabilization		
Medication	**Dose Range**	**Comment**
Inamrinone	0.75–1 mg/kg IV/IO over 5 minutes; may repeat × 2 then: 5–10 mcg/kg per minute	Inodilator
Dobutamine	2–20 mcg/kg per minute IV/IO	Inotrope; vasodilator
Dopamine	2–20 mcg/kg per minute IV/IO	Inotrope; chronotrope; renal and splanchnic vasodilator in low doses; pressor in high doses
Epinephrine	0.1–1 mcg/kg per minute IV/IO	Inotrope; chronotrope; vasodilator in low doses; pressor in higher doses
Milrinone	Loading dose: 50 mcg/kg IV/IO over 10–60 min then 0.25–0.75 mcg/kg per minute	Inodilator
Norepinephrine	0.1–2 mcg/kg per minute	Vasopressor
Sodium nitroprusside	Initial: 0.5–1 mcg/kg per minute; titrate to effect up to 8 mcg/kg per minute	Vasodilator Prepare only in D_5W

- IV indicates intravenous; and IO, intraosseous.
- Alternative formula for verifying dose during continuous infusion:
- Infusion rate

$$(\text{mL/h}) = \frac{[\text{weight (kg)} \times \text{dose (mcg/kg per min)} \times 60\ (\text{min/hour})]}{\text{concentration(mcg/mL)}}.$$

American heart association 2015

3- Neurologic System

For infants and children remaining comatose after OHCA, it is reasonable either to maintain 5 days of continuous normothermia (36°C to 37.5°C) or to maintain 2 days of initial continuous hypothermia (32°C to 34°C) followed by 3 days of continuous normothermia

Fever (temperature 38°C or higher) should be aggressively treated after ROSC

Table (3): Glasgow coma scale *(nelson 20th edition)*

Eye opening (total possible points 4)			
Spontaneous	4		
To voice	3		
To pain	2		
None	1		
Verbal response (total possible points 5)			
Older children		**Infants and young children**	
Oriented	5	Appropriate words, smile, fixes and follows	5
Confused	4	Consolable crying	4
Inappropriate	3	Persistently irritable	3
Incomprehensible	2	Restless, agitated	2
None	1	none	1
Motor response (total possible points 6)			
Obeys	6		
Localizes pain	5		
Withdraw	4		
Flexion	3		
Extension	2		
None	1		

4- Renal System

Decreased urine output (<1 mL/kg per hour in infants and children or <30 mL/hour in adolescents) may be caused by prerenal conditions (eg, dehydration, inadequate systemic perfusion), renal ischemic damage, or a combination of factors. Avoid nephrotoxic medications and adjust the dose of medications excreted by the kidneys until you have checked renal function

References:

American Heart Association. Web-based Integrated Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care – Part 12: Pediatric Advanced Life Support. ECCguidelines.heart.org.

American Heart Association. Web-based Integrated Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care – Part 11: Pediatric Basic Life Support and Cardiopulmonary Resuscitation Quality. ECCguidelines.heart.org

Shock

Definition: Shock is an acute process characterized by the body's inability to deliver adequate oxygen to meet the metabolic demands of vital organs and tissues.

Table (4): Types of shock *(nelson 20th edition)*

Hypovolemic	Cardiogenic	Distributive	Septic	Obstructive
Decreased preload secondary to internal or external losses	Cardiac pump failure secondary to poor myocardial function	Abnormalities of vasomotor tone from loss of venous and arterial capacitance	Encompasses multiple forms of shock Hypovolemic; third spacing of fluids into the extracellular, interstitial space Distributive: early shock with decreased afterload Cardiogenic; depression of myocardial function by endotoxins	Decreased cardiac output secondary to direct impediment to right- or left-heart outflow or restriction of all cardiac chambers
Potential etiologies Blood loss: hemorrhage; Plasma loss: burns, nephrotic syndrome; Water/electrolyte loss: vomiting diarrhea	Congenital heart disease Cardiomyopathies: infectious or acquired, dilated or restrictive Ischemia Arrhythmias	Anaphylaxis Neurologic: loss of sympathetic vascular tone secondary to spinal cord or brainstem injury Drugs	Bacterial Viral Fungal (Immunocompromised patients are at increased risk)	Tension pneumothorax Pericardial tamponade Pulmonary embolism Anterior mediastinal masses Critical coarctation of the aorta

Table (5): Hemodynamic variables in different shock states *(nelson 20th edition)*

Type of shock	Cardiac output	Systemic vascular resistance	Mean arterial pressure	Capillary wedge pressure	Central venous pressure
Hypovolemic	↓	↑	↔ or ↓	↓↓↓	↓↓↓
Cardiogenic*					
Systolic	↓↓	↑↑↑	↔ or ↓	↑↑	↑↑
Diastolic	↔	↑↑	↔	↑↑	↑
Obstructive	↓	↑	↔ or ↓	↑↑♦	↑↑♦
Distributive	↑↑	↓↓↓	↔ or ↓	↔ or ↓	↔ or ↓
Septic					
Early	↑↑↑	↓↓↓	↔ or ↓□	↓	↓
Late	↓↓	↓↓	↓↓	↑	↑ or ↔

* Systolic or diastolic dysfunction
♦ Wedge pressure, central venous pressure, and pulmonary artery diastolic pressures are equal
□ Wide pulse pressure

Sepsis

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (new definition JAMA 2016).
- Organ dysfunction can be identified as an acute change in total SOFA score 2 points consequent to the infection.
- The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.

SOFA score

Table (6): Sequential [Sepsis-related] organ failure assessment score *(JAMA 2016)*

System	Score 0	1	2	3	4
Respiration PaO_2/FiO_2, mmHg (kPa)	≥ 400 (53.3)	< 400 (53.3)	< 300 (40)	< 200 (26.7) with respiratory support	< 100 (13.3) with respiratory support
Coagulation Platelets, $*10^3/\mu l$	≥ 150	< 150	< 100	< 50	< 20
Liver Bilirubin, mg/dL (µmol/L)	< 1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	> 12.0 (204)
Cardiovascular	MAP ≥ 70 mm.Hg	Dopamine < 5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1[b]	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1[b]	
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	< 6
Renal Creatinine, mg/dL (µmol/L)	< 1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	> 5.0 (440)
Urine output, mL/d				< 500	< 200

qSOFA score

- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, ie, alteration in mental status, systolic blood pressure 100 mm Hg, or respiratory rate 22/min.

Box 4. qSOFA (Quick SOFA) Criteria *(JAMA 2016)*

- Respiratory rate ≥ 22/min.
- Altered mentation
- Systolic blood pressure ≤ 100 mmHg

Septic shock

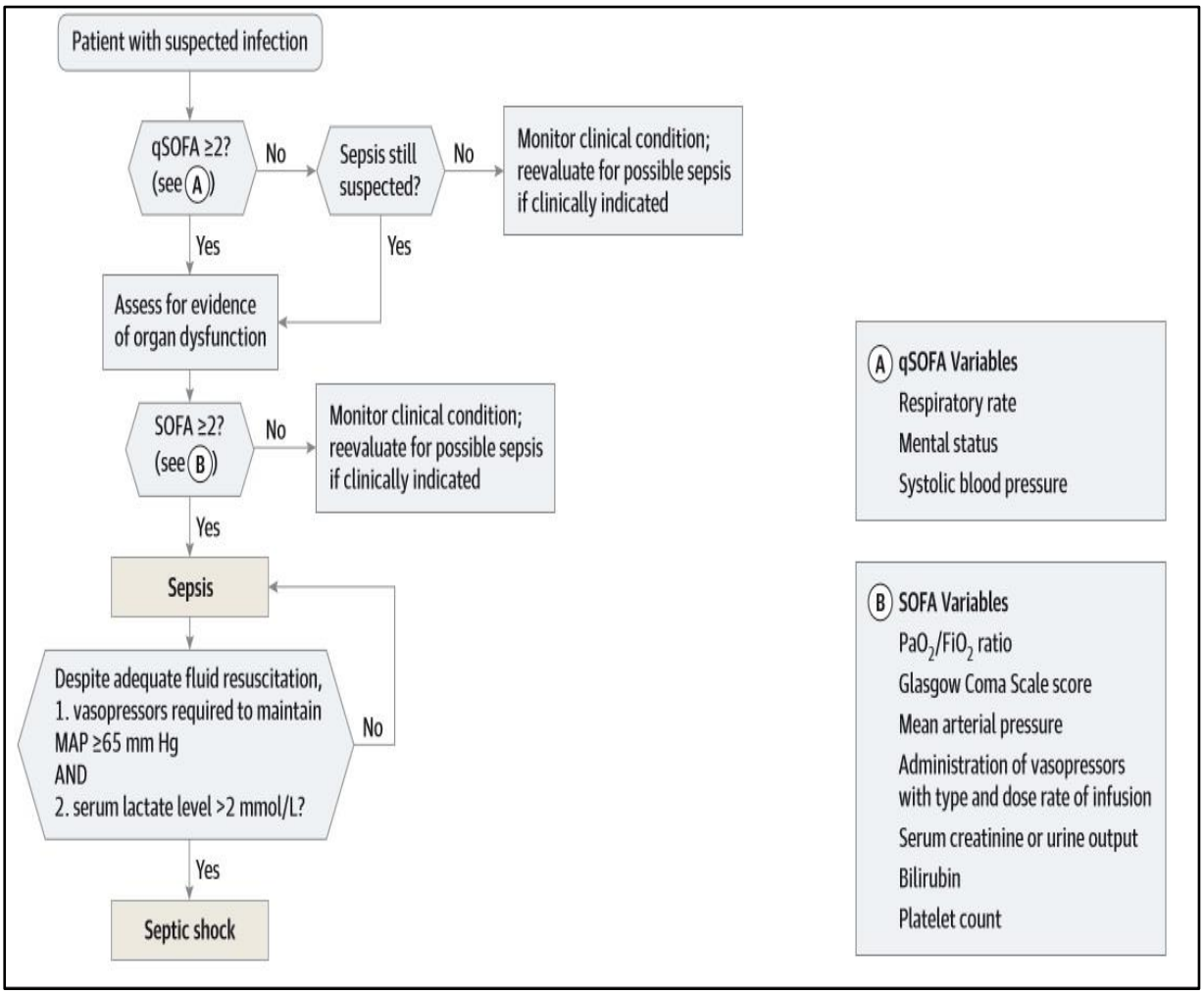
• Septic shock is a subset of sepsis in which underlying circulatory and cellular/ metabolic abnormalities are profound enough to substantially increase mortality.

• ***Patients with septic shock can be identified*** with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP 65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.

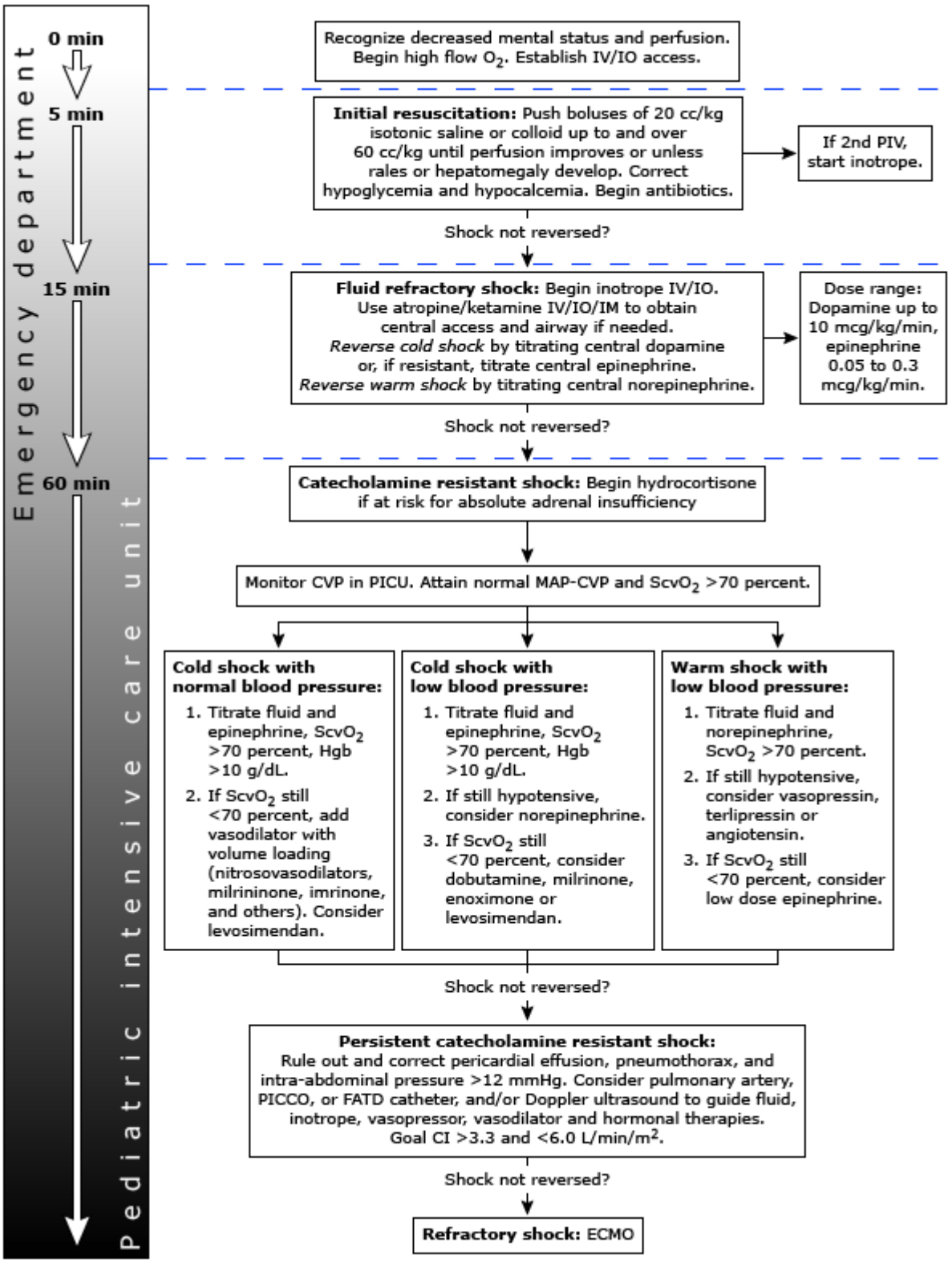
How to differentiate between cold and warm shock?

	Cold shock	Warm shock
Capillary refill	> 2 seconds	Flash capillary refill
Peripheral pulses	Diminished	Bounding
Mottling of skin	Present	Absent

How to proceed? *(JAMA 2016)*



Management of septic shock *(nelson 20th edition)*



Early goal directed therapy:

During the first 6 hours of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as one part of a treatment protocol:

- Central venous pressure (CVP) 8-12 mm Hg
- Mean arterial pressure (MAP) ≥65 mm Hg
- Urine output ≥0.5 mL/kg/hr
- Central venous (superior vena cava) or mixed venous oxygen saturation ≥70 percent or ≥65 percent, respectively

(The 2012 Surviving Sepsis Campaign Guidelines)

Therapeutic endpoints

Clinical

- Heart Rate normalized for age
- Capillary refill < 2sec
- Normal pulse quality
- Warm extremities
- Blood pressure normal for age
- Urine output >1 mL/kg/h
- Normal mental status
- CVP >8 mmHg
- No difference in central and peripheral pulses

Threshold rates	Heart rate (bpm)	Mean arterial pressure
Term newborn	120-180	55
Up to 1 yr	120-180	60
Up to 2 yrs	120-160	65
Up to 7 yrs	100-140	65
Up to 15 yrs	90-140	65

Laboratory

- Decreasing lactate
- SvO2 >70%

Table (7): Vasodilators/Afterload reducers *(nelson 20th edition)*

Drug	Effect(s)	Dosing range	Comment(s)
Nitroprusside	Vasodilator (mainly arterial)	0.5-4.0 μg/kg/min	Rapid effect Risk of cyanide toxicity with prolonged use (> 96 hr)
Nitroglycerin	Vasodilator (mainly venous)	1-20 μg/kg/min	Rapid effect Risk of increased intracranial pressure
Prostaglandin E_1	Vasodilator Maintains an open ductus arteriosus in the newborn with ductal-dependent congenital heart disease	0.01-0.2 μg/kg/min	Can lead to hypotension Risk of apnea
Milrinone	Increased cardiac contractility Improves cardiac diastolic function Peripheral vasodilation	Load 50 μg/kg over 15 min 0.5-1.0 μg/kg/min	Phosphoodiesterase inhibitor – slows cyclic adenosine monophosphate breakdown

Table (8): Cardiovascular drug treatment of shock *(nelson 20th edition)*

Drug	Effect(s)	Dosing range	Comment(s)
Dopamine	↑ Cardiac contractility	3-20 μg/kg/min	↑ Risk of arrhythmias at high doses
	Significant peripheral vasoconstriction at > 10 μg/kg/min		
Epinephrine	↑ Heart rate and ↑ cardiac contractility Potent vasoconstrictor	0.05-3.0 μg/kg/min	May ↓ renal perfusion at high doses ↑ Myocardial O_2 consumption Risk of arrhythmia at high doses
Dobutamine	↑ Cardiac contractility Peripheral vasodilator		
Norepinephrine	Potent vasoconstriction No significant effect on cardiac contractility	0.05-1.5 μg/kg/min	↑ Blood pressure secondary to ↑ systemic vascular resistance ↑ Left ventricular afterload
Phenylephrine	Potent vasoconstriction	0.05-2.0 μg/kg/min	Can cause sudden hypertension ↑ O_2 consumption

Terlipressin dose in septic shock:

There are multiple clinical trials but there is no dose evidence based yet.

Rodriguez-Nunez et al., 2006 recommend dose of ***20 μ/kg/dose every 4 hours*** it results in increasing MAP, reduction of catecholamine infusion.

References:

- David A. Turner and Ira M. Cheifetz, shock Chapter 70 Part IX 516:528 nelson textbook of pediatrics 20th edition 2015
- Mervyn Singer, Clifford S. Deutschman, Christopher Warren Seymour, Manu Shankar-Hari, Djillali Annane, Michael Bauer et al., The Third International Consensus Definitions for Sepsis and Septic Shock(Sepsis-3) JAMA.2016; 315(8):801-810.
- Rodriguez-Nunez A, Lopez-Herce J, GilAntonJ, et al: Rescue treatment with terlipressin in children with refractory septic shock: A clinical study. Crit Care 2006; 10: R20 (doi:10.1186/cc3984)

Anaphylactic shock

Emergency treatment

- Patients with anaphylaxis should be placed on their back with lower extremities elevated. If short-of-breath and/or vomiting, patient should be placed semi-upright in a position of comfort with the lower extremities elevated.

- Intramuscular epinephrine 1: 1000 (1 mg/ml) at a dose of 0.01 mg/kg body weight up to a maximum dose of 0.3 mg injected into the lateral thigh (vastus lateralis).

- The dose can be repeated at 5-15 min intervals.

- The intramuscular route is preferred because epinephrine has a vasodilator effect in skeletal muscle. After IM injection into the vastus lateralis, absorption is rapid, and epinephrine reaches the central circulation rapidly.

- The maximum dose of epinephrine in anaphylaxis is lower than the dose used in cardiopulmonary resuscitation.

- Failure to inject it promptly before the patient gets acute cardio-respiratory failure and shock potentially increases the risk of death and the risk of biphasic anaphylaxis (late phase reaction).

- Support the airway and ventilation

- Give supplementary oxygen 6-8 L/min

- Resuscitate with intravenous saline 0.9% (20 ml/kg body weight, repeated up to a total of 50 ml/kg over the first half an hour.

- Other lines of treatment:

¯ Nebulized beta-2 stimulants: Decrease wheeze but are not life-saving ¯ H1-antihistamines: Decrease itch and hives but not life saving

Dose of diphenhydramine (Pirafene 50 mg/ml):

2-6 years: 6.25 mg 6-12 years: 12.2-25 mg > 12 years: 25-50 mg

- Corticosteroids: effects take several hours: not lifesaving. Used to prevent biphasic; however, there is no evidence that this occurs.

Dose of solucortif: 2.5- 5mg / kg

- **Refractory cases:**

  - ***IV epinephrine:*** central line – 1:10,000 solution – infusion pump - Intubation

  - ***Cricothyrotomy***

  - ***Vasopressors***

  - ***Glucagon:*** exerts positive inotropic and chronotropic effects on the heart, independent of catecholamines. Therefore, glucagon, 1 mg intravenous bolus, followed by an infusion of 1 to 5 mg per hour, may improve hypotension in one to five minutes, with a maximal benefit at five to 15 minutes. (The U.S. Food and Drug Administration have not approved glucagon for this use.) Nausea and vomiting may limit therapy with glucagon.

- **Duration of monitoring**

  - Protracted or biphasic anaphylaxis (up to 72 hours; usually within 10 hours) occurs in up to 20% of adults and 6% of children. - Patients should ideally be monitored for at least 4, and preferably 8-10 hr.

  - Some cases require monitoring for ≥ 24 hours.

Place the patient on their back with lower extremities elevated.

If short-of-breath and/or vomiting, patient should be placed semi-upright in a position of comfort with the lower extremities elevated.

↓

Adrenaline I.M

1: 1000 (1 mg/ml) at a dose of 0.01 mg/kg body weight up to a maximum dose of 0.3 mg injected into the lateral thigh (vastus lateralis)

↓

Support the airway and ventilation

Give supplementary oxygen 6-8 L/min

↓

Resuscitate

Intravenous saline 0.9% (20 ml/kg body weight, repeated up to a total of 50 ml/kg over the first half an hour.

↓

Other lines of treatment (not lifesaving)

Nebulized beta-2 stimulants | H1-antihistamines | Corticosteroids

↓

Refractory cases

IV epinephrine: central line – 1:10,000 solution – infusion pump

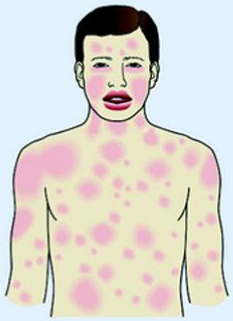
- ***Intubation***
- ***Cricothyrotomy***
- ***Vasopressors***: noradrenaline or dopamine
- ***Glucagon:***

Acknowledgment:

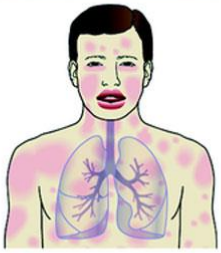
- Thanks to **Prof. Dr. Elham Hosni**, for participating in this chapter.

Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:

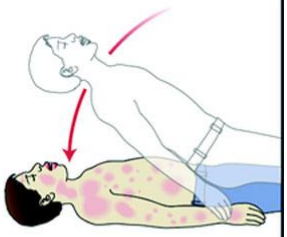
1 **Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)**



AND AT LEAST ONE OF THE FOLLOWING:

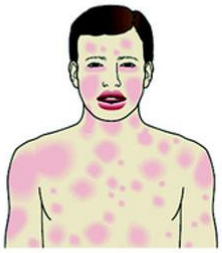


Sudden respiratory symptoms and signs (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)

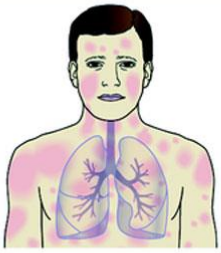


Sudden reduced BP or symptoms of end-organ dysfunction (e.g. hypotonia [collapse], incontinence)

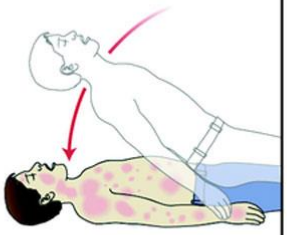
OR **2** **Two or more of the following that occur suddenly after exposure to a *likely allergen or other trigger* for that patient* (minutes to several hours):**



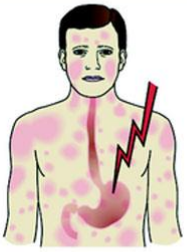
Sudden skin or mucosal symptoms and signs (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)



Sudden respiratory symptoms and signs (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)



Sudden reduced BP or symptoms of end-organ dysfunction (e.g. hypotonia [collapse], incontinence)



Sudden gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)

OR **3** **Reduced blood pressure (BP) after exposure to a *known allergen** for that patient* (minutes to several hours):**

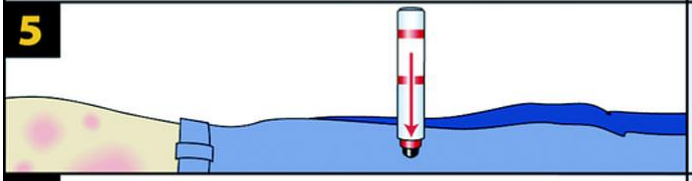
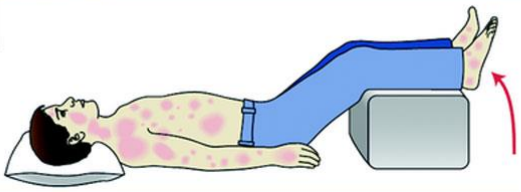
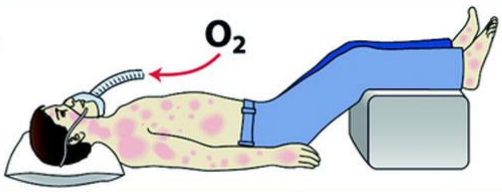
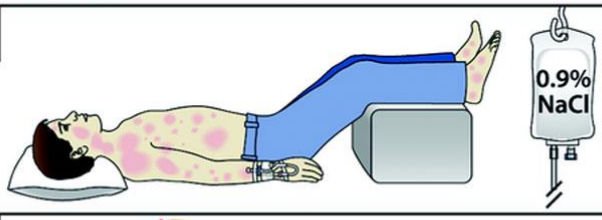
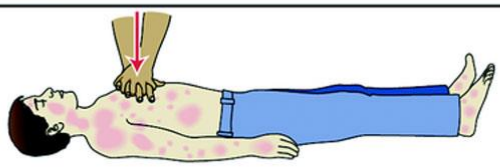
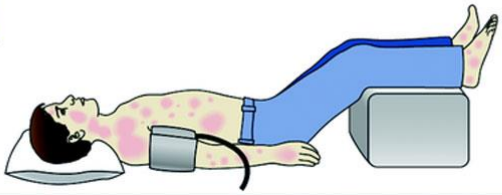
Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP***

Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

* For example, immunologic but IgE-independent, or non-immunologic (direct mast cell activation)

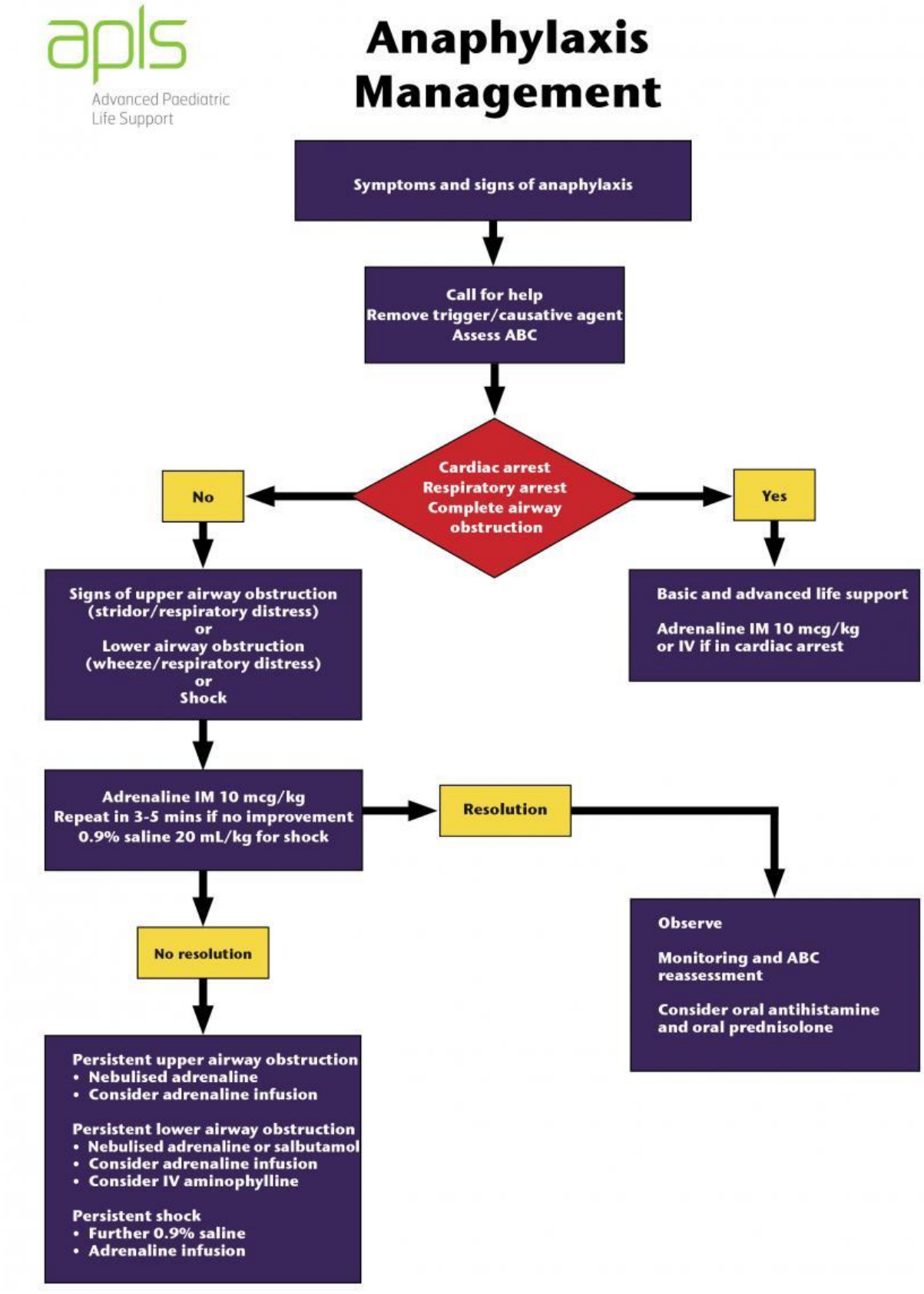
** For example, after an insect sting, reduced blood pressure might be the only manifestation of anaphylaxis; or, after allergen immunotherapy, generalized hives might be the only initial manifestation of anaphylaxis.

*** Low systolic blood pressure for children is defined as less than 70 mm Hg from 1 month to 1 year, less than (70 mm Hg + [2 x age]) from 1 to 10 years, and less than 90 mm Hg from 11 to 17 years. Normal heart rate ranges from 80-140 beats/minute at age 1-2 years; from 80-120 beats/minute at age 3 years; and from 70-115 beats/minute after age 3 years. In infants and children, respiratory compromise is more likely than hypotension or shock, and shock is more likely to be manifest initially by tachycardia than by hypotension.

1	**Have a written emergency protocol** for recognition and treatment of anaphylaxis and rehearse it regularly.	
2	**Remove exposure to the trigger** if possible, eg. discontinue an intravenous diagnostic or therapeutic agent that seems to be triggering symptoms.	
3		**Assess the patient's circulation, airway, breathing, mental status, skin, and body weight** (mass).
		Promptly and simultaneously, perform steps 4, 5 and 6.
4		**Call for help:** resuscitation team (hospital) or emergency medical services (community) if available.
5		**Inject epinephrine** (adrenaline) intramuscularly in the mid-anterolateral aspect of the thigh, 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution, maximum of 0.5 mg (adult) or 0.3 mg (child); **record the time of the dose and repeat it** in 5-15 minutes, if needed. Most patients respond to 1 or 2 doses.
6		**Place patient on the back** or in a position of comfort if there is respiratory distress and/or vomiting; **elevate the lower extremities;** fatality can occur within seconds if patient stands or sits suddenly.
7		**When indicated, give high-flow supplemental oxygen** (6-8 L/minute), by face mask or oropharyngeal airway.
8		**Establish intravenous access** using needles or catheters with wide-bore cannulae (14 - 16 gauge). **When indicated, give 1-2 litres of 0.9% (isotonic) saline rapidly** (e.g. 5-10 mL/kg in the first 5-10 minutes to an adult; 10 mL/kg to a child).
9		**When indicated at any time, perform cardiopulmonary resuscitation** with continuous chest compressions.
		In addition,
10		**At frequent, regular intervals, monitor patient's blood pressure, cardiac rate and function, respiratory status, and oxygenation** (monitor continuously, if possible).

- **Reference:**

Simons FER et al., for the WAO. J Allergy Clin Immunol 2011; 127: 587-93-e22 and WAO Journal 2011; 4: 13-36. Illustrator: J Schaffer



Fluid and Electrolytes Management

This section includes:

1. Assessment of Hydration
2. Resuscitation
3. Risk of Acute Kidney Injury (AKI)
4. Fluid Requirements
5. Hyponatraemia
6. Hypernatraemia
7. Hyperkalaemia
8. Hypokalaemia

1-Assessment of Hydration

The clinical assessment of hydration is difficult and often inaccurate. In children who are dehydrated the accepted gold standard of assessment is acute weight loss but this is often not possible due to lack of accurate pre-illness weight.

The following table can be used to help make an assessment of hydration status:-

Table (9): Assessment of hydration status *(Fluid and Electrolyte Disturbances, Nottingham children's university November 2015)*

Clinical Sign	No dehydration (<3% weight loss	Mile to Moderate 3-10%	Severe > 10%	Notes
Reduced urine output	No	Yes	Yes	Take care to differentiate urine from watery stool
Dry mouth	No	Yes	Yes	Mouth breathers may have dry mouth
Sunken eyes	No	Yes	Yes	
Reduced skin turgor	No (recoils instantly)	Yes (1-2 secs)	Yes (> 2 secs)	Less in hypernatraemic dehydration
Prolonged capillary refill time	No	Might be slightly prolonged	Yes Cool / mottled / pale peripheries	CRT < 2 seconds may be seen as 'normal'
Drowsiness/ Irritability	No	Yes	Severe	

2-Resuscitation

- If signs of circulatory collapse are present i.e. prolonged capillary refill time, tachycardia and/or hypotension then immediate resuscitation of intravascular volume must occur.
- This should be via intravenous or intraosseous access.
- Boluses of 20 ml/kg 0.9% sodium chloride (isotonic solution) should be used.
- Reassessment and repeat boluses given as necessary with consideration of the cause of circulatory collapse i.e. blood loss, sepsis so that alternative resuscitation fluids can be considered if appropriate.

3-Risk of Acute Kidney Injury (AKI)

Certain children and young people are particularly at risk of developing AKI. Measurement of serum creatinine and comparison with baseline should be undertaken in children and young people with acute illness and any degree of dehydration if any of the following are likely or present:

- Young age, neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a parent or carer with hypovolaemia
- Chronic kidney disease / transplant
- Heart failure
- Liver disease
- Past history of acute kidney injury
- Oliguria (urine output less than 0.5 ml/kg/hour)
- Use of drugs with nephrotoxic potential (such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs and diuretics) within the past week
- Symptoms or history of urological obstruction, or conditions that may lead to obstruction
- Sepsis
- Hematological malignancy
- Hypotension.

4-Fluid Requirements

- **Calculation of maintenance fluid requirements**
  - 100mls/kg for the first 10kg = 1000mls
  - 50mls/kg for the second 10kg = 500mls
  - 20mls/kg for all additional Kg

- **Dehydration**

  Fluid deficit in ml = % dehydration x weight (Kg) x 10

  Mild dehydration: 50 ml / kg

  Moderate dehydration: 80 ml / kg

  Severe dehydration: 100 ml / kg

Fluid management of dehydration

- Restore intravascular volume

  Normal saline:-20ml/kg over 20min

  Repeat as needed
- Calculate 24-hr fluid needs:-maintenance +deficit volume
- Subtract isotonic fluid already administrated from 24hr fluid needs
- Administrate remaining volume over 24 hr using 5% dextrose NS+20meq/L KCL
- Replace ongoing losses as they occur

Replacement fluid for diarrhea

- Average composition of diarrhea

  Sodium :25mEq/l Potassium :25mEq/l Bicarbonate:15meq/l
- Approach to replacement of ongoing losses

  Solution: D5 1/2 NS +30 mEq/l sodium bicarbonate +20 mEq/L KCL
- Replace stool ml/ml every 1-6 hr

Replacement fluid for emesis or nasogastric losses:

- Average composition of gastric fluid:

  Sodium 60 mEq/L Potassium: 10mEq/L Chloride: 90mEq/L
- Approach to replacement of ongoing losses:

  Solution: normal saline + 10 mEq/L KCL
- Replace output mL/mL every 1-6 hours

Adjusting fluid therapy for altered renal output

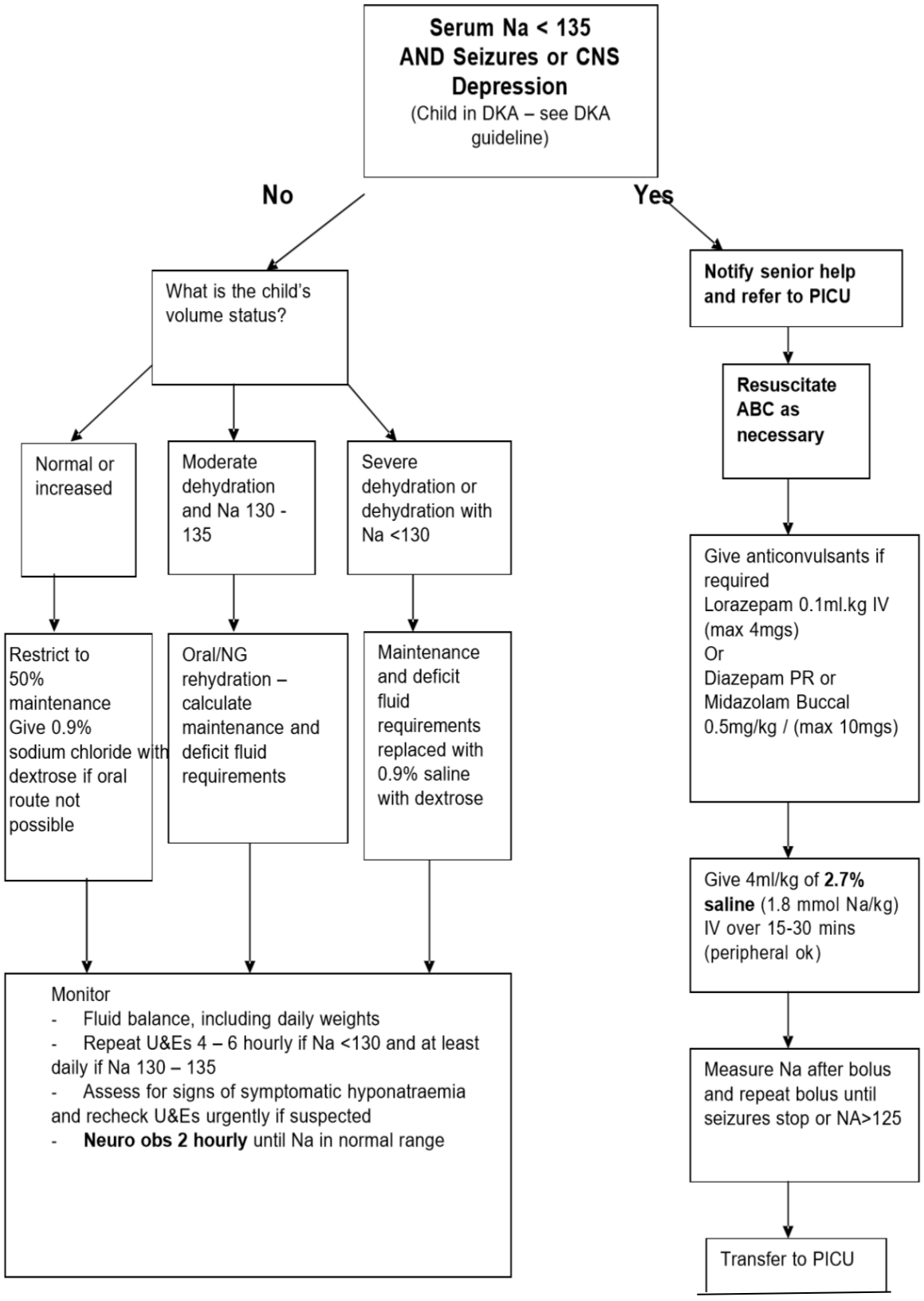
- Replacement of insensible fluid losses (25-40% of maintenance) with D5 $^{1}/_{2}$ NS
- Replace urine output mL/mL with D5 $^{1}/_{2}$ NS ± KCL

Hypernatremic dehydration:

Treatment of hypernatremic dehydration

- Restore intravascular volume:
  Normal saline: 20 mL/Kg over 20 min (repeat until intravascular volume restored)
- Determine time for correction on basis of initial sodium concentration:
  - Na 145-157 mEq/L : 24 hr
  - Na 158-170 mEq/L : 48 hr
  - Na 171-183 mEq/L : 72 hr
  - Na 184-196 mEq/L : 84 hr
- Administer fluid at constant rate over time for correction:
  - Typical fluid: 5% dextrose + half normal saline (with 20 mEq/L KCL unless contraindicated)
  - Typical rate: 1.25-1.5 times maintenance
- Follow serum sodium concentration
- Adjust fluid on basis of clinical status and serum sodium concentration:
  - Signs of volume depletion: administer normal saline (20 mL/Kg)
  - Sodium decreases too rapidly; either:
    - Increase sodium concentration of intravenous fluid ***or***
    - Decrease rate of intravenous fluid
  - Sodium decreases too slowly; either
    - Decrease sodium concentration of intravenous fluids ***or***
    - Increase rate of intravenous fluid
- Replace ongoing losses as they occur
- Avoid rapid correction allow rate of decent not more than 10-12 mEq/L/day

Management of Hyponatraemia



Hypokalemia:

- The dose of intravenous potassium is 0.5-1 mEq/kg, usually given over 1 hr. The adult maximum dose is 40 mEq.

Hypokalemia produces one of the least specific ECG changes:

Cardiac monitoring should be considered in patients with a K+ < 3 mmol/l

1. Prominent U wave.
2. ST segment depression.
3. Flat, low or diphasic T waves.

   Normal T wave amplitude in V5: <1year 11mm >1year 14mm

   V6: <1year 7mm >1year 9mm

4. With further lowering of K+ the PR interval may become prolonged and sinoatrial block may occur

Potassium administration:

Potassium chloride is always given by IV infusion,NEVER by bolus injection.

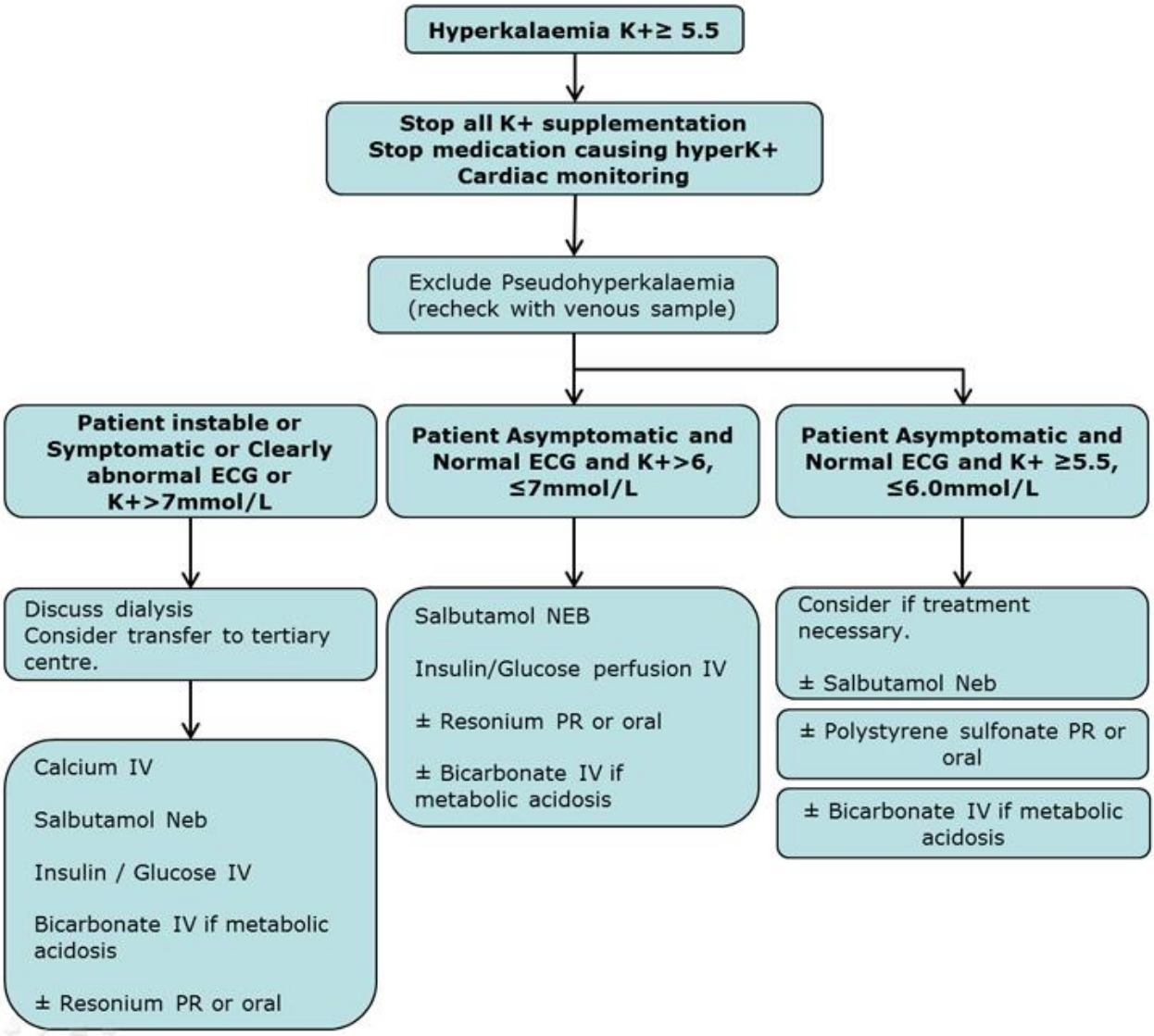
• Maximum concentration via a peripheral vein is usually 40mEq /L can be increased to 60mEq/L after consultant recommendation.

• Maximum concentration via a central vein is usually 150mEq /L can reach 200mEq/L in severely restricted patients

*The maximum infusion rate via peripheral line is 0.5- 1mEq/kg / hour should not exceed 10mEq/hour

* The maximum infusion rate via central line is 1mEq/ kg / hour should not exceed 20mEq/hour

Management of hyperkalemia:



Management of hyperkalemia:

- Level of potassium should be confirmed with a second sample.
    - If patient present renal dysfunction (renal failure or other renal disease), assume potassium level correct until proven otherwise
    - Acute increases of potassium means higher risk of arrhythmia.

- Do an ECG to identify conduction disturbance:
    - Peaked T wave (early)
    - Prolonged PR, flattening of P wave, widening of QRS(increased risk of arrhythmia)
    - Absence of P wave, Sine wave (fusion of QRS and T wave)
    - Ventricular arrhythmia, asystole

- Complete your investigation and search for causes of hyperkalaemia:
    - Urea, creatinine and electrolytes
    - Glucose
    - Venous blood gas
    - +/- Urine analysis and urinary electrolytes

- Consider other investigations depending on cause:
    - CK
    - Cortisol, aldosterone and hormonal precursor levels (particularly if hypoNa+)

Table (10): Drug dosage for treatment of hyperkalemia

Name of drug	Dose	onset of action	Duration
I.V calcium:	Calcium Gluconate 10%: 0.5 ml/kg slow IV injection over 2-5 minutes if unstable, over 15-20min if stable (Max: 20ml)	<3 minutes, should see normalization of ECG. If not: repeat dose (twice)	~30 minutes
	Note: Give under cardiac monitoring, discontinue if HR dropping significantly, Avoid extravasations **NOT to be given simultaneously with bicarbonate, NOT to be given if digitalis toxicity**		
Salbutamol nebulization:	*Less than 25kg : 2.5 mg neb q 1-2h *More than 25kg : 5mg neb (Adult max 10-20mg) q 1-2h	30 minutes, should reduce intravascular K+ of 0.5-1.5mmol/L	2-3 hours
INSULIN/GLUCOSE to be given at the same time	***If SEVERE HYPERKALAEMIA:*** *Dextrose 10% : 5ml/kg IV bolus (if no hyponatremia) *Insulin short action: 0.1 U/kg IV bolus (Max 10 units) ***Then followed by infusion insulin/glucose*** ***If MODERATE HYPERKALAEMIA:*** *Dextrose 10% IV at maintenance with 0.9% sodium chloride (normal saline) *Insulin short action infusion : 0.1 U/kg/h IV	15 minutes, should reduce intravascular K+, reduction of 0.5-1.5mmol/L	peak 60 minutes till 2-3hours
	Close monitoring of glucose every 30-60 minutes		
BICARBONATE In metabolic acidosis only.	***SEVERE HYPERKALAMIA and metabolic acidosis*** •Sodium Bicarbonate 8.4% 1mmol/ml : 1-3ml/kg IV over 5 minutes ***MILD TO MODERATE HYPERKALAEMIA and metabolic acidosis:*** •Sodium Bicarbonate 8.4% 1mmol/ml : 1ml/kg in slow IV infusion over 30 minutes	30-60 minutes, should reduce intravascular K+ of 0.5	2-3 hours
	NOT to give simultaneously with Calcium		
•Polystyrene sulfonate (sorbisterit)	0.3-1g/kg q 6h (Max 15-30g) PR or oral (with lactulose)	1h PR, 4-6h oral, should reduce intravascular K+ of 0.5-1 mEq/L	variable
	NOT to be used if ileus, recent abdominal surgery, perforation, hypernatremia		

Table (11): Different types of intravenous fluids *(pediatric nephrology text book 7th edition)*

Fluid	Osmolarity (mOsm/l)	Na (mEq/l)	K (mEq/l)	Cl (mEq/l)	Buffer (source) (mEq/l)	Mg (mEq/l)	Ca (mEq/l)	Dextrose (g/l)
Crystalloids								
0.9 % saline	308	154	0	154	0	0	0	0
Lactated Ringer's	275	130	4	109	28 (lactate)	0	3	0
D5 0.45 % saline	454	77	0	77	0	0	0	50
D5 0.22 % saline	377	38	0	38	0	0	0	50
5 % dextrose water	252	0	0	0	0	0	0	50
Normosol	295	140	5	98	27 (acetate) 23 (gluconate)	3	0	0
Plasma-Lyte	294	140	5	98	27 (acetate) 23 (gluconate)	3	0	0
Colloids								
5 % albumin	309	130–160	<1	130–160	0	0	0	0
25 % albumin	312	130–160	<1	130–160	0	0	0	0
Fresh frozen plasma	300	140	4	110	25 (bicarbonate)	0	0	0
3.5 % Haemaccel	301	145	5	145	0	0	6	0
6 % hetastarch	310	154	0	154	0	0	0	0
Dextran 40 or 70	310	154	0	154	0	0	0	0

Table (12): Different types of intravenous fluids

Fluid	Fluid type[a]	Osmolality (compared with plasma)	Tonicity (with reference to cell membrane)	Sodium content (mmol/ litre)	Potassium content (mmol/ litre)
Isotonic crystalloids that contain sodium in the range 131–154 mmol/litre	0.9% sodium chloride	Isosmolar	Isotonic	154	0
	Hartmann's solution	Isosmolar	Isotonic	131	5
Isotonic crystalloids with glucose that contain sodium in the range 131–154 mmol/litre	0.9% sodium chloride with 5% glucose	Hyperosmolar	Isotonic	150	0
Hypotonic fluids	0.45% sodium chloride with 5% glucose	Hyperosmolar	Hypotonic	75	0
	0.45% sodium chloride with 2.5% glucose	Isosmolar	Hypotonic	75	0
	0.45% sodium chloride	Hyposmolar	Hypotonic	75	0
	5% glucose	Isosmolar	Hypotonic	0	0
	10% glucose	Hyperosmolar	Hypotonic	0	0

N.B:

0.9% sodium chloride with 5% glucose fluid is isotonic fluid but hyperosmolar is used in deficit therapy and to treat hyponatremia it's not commercially available in our hospitals so it can be replaced by fluid cocktail made as follows

Hypertonic saline 3%: glucose 5% by concentration 1:3

Giving Na 130mEq/L and glucose 3.7%

References:

- The Royal Children's Hospital Melbourne, Clinical Practice Guidelines of hypokalemia march 2016
- Standards for Pediatric Intravenous Fluids: NSW Health (second edition) august 2015
- Intravenous fluid therapy in children and young people in hospital NICE guideline Published: 9 December 2015 nice.org.uk/guidance/ng29
- Fluid and Electrolyte Disturbances, Nottingham children's university November 2015
- Nelson text book of pediatrics 20th edition 2015 chapter 57 deficit therapy

Acute Severe Asthma

Management of acute severe asthma in ER:

Initial management:

- Routine vital signs and check saturation, blood pressure and height
- Perform Pediatric Asthma Score (PAS)

Table (13): Pediatric intensive care unit pediatric asthma score *(Nievas et al 2013)*

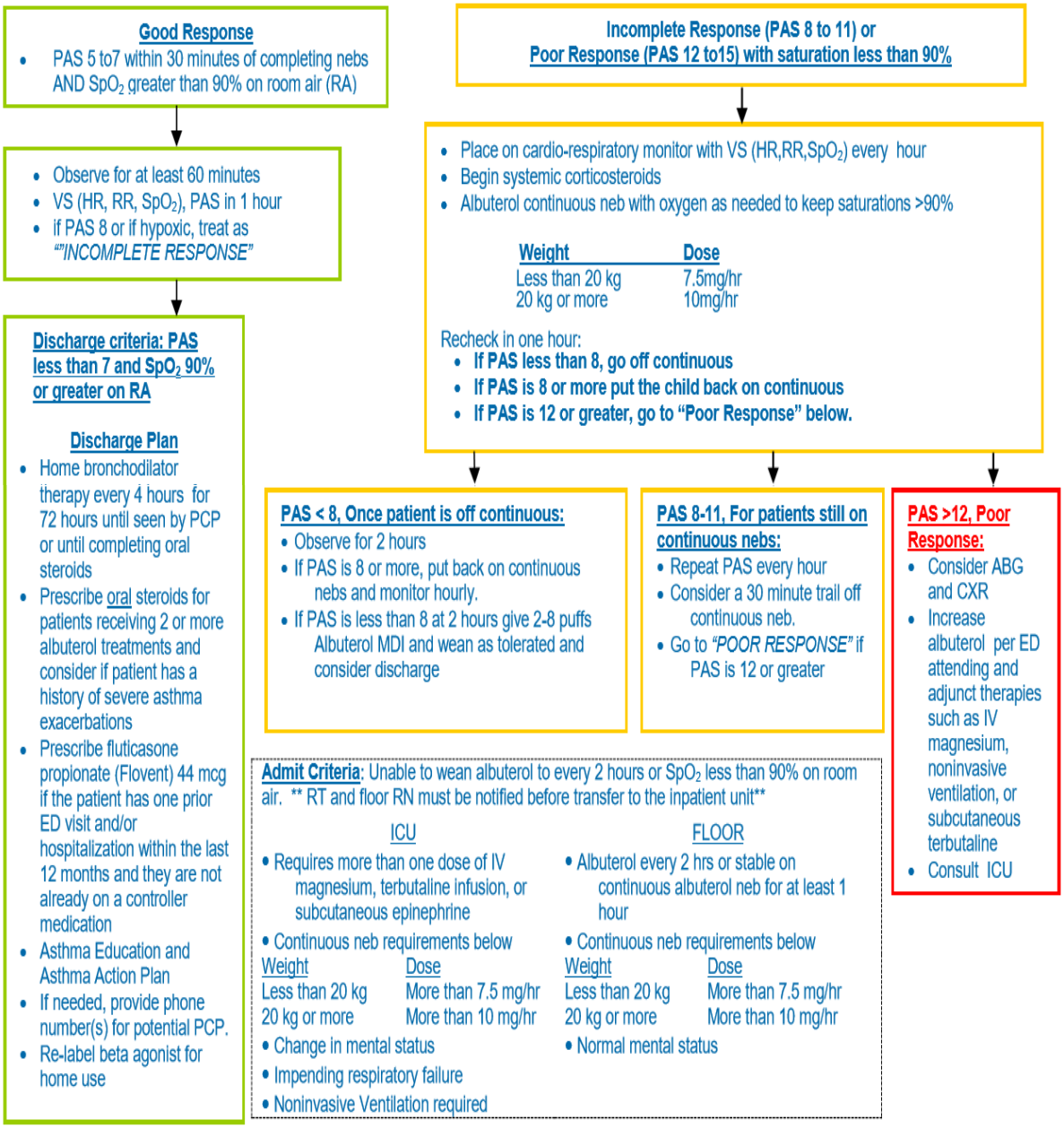
Examination component	1	2	3
Respiratory rate			
1-4 y	≤34	35-39	≥40
4-6 y	≤30	31-35	≥36
6-12 y	≤26	27-30	≥31
>12 y	≤23	24-27	≥28
O_2 requirement	>95% on room air	90%-95% on room air	<90% on room air or any oxygen
Retractions	None or intercostal	Intercostal and substernal	Intercostal, substernal, and supraclavicular
Work of breathing (count to 10)	Speaks in sentences, coos and babbles	Speaks in partial sentences, short cry	Speaks in single words/short phrases, grunting
Auscultation	Normal breath sounds to end-expiratory wheezes only	Expiratory wheezing	Inspiratory and expiratory wheezing to diminished breath sounds

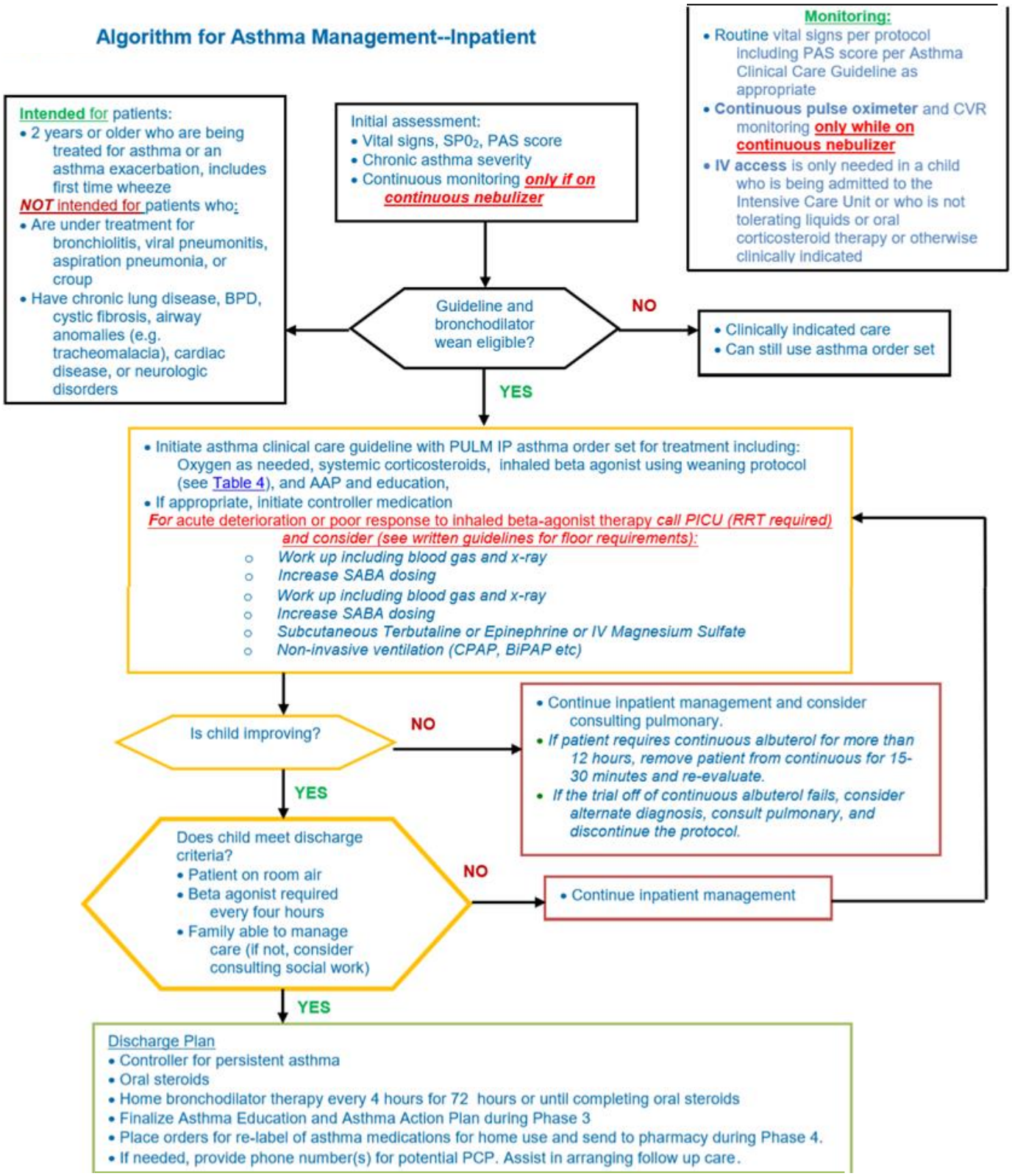
- Oxygen to keep SpO2 greater than 90%
- Give combination ipratropium bromide 0.5 mg nebulized with albuterol (weight specific dosing below) for a total of up to three initial treatments

Weight	Dose	Frequency
Less than 20 kg	2.5 mg = 0.5 ml	3 times
20 kg or more	5 mg =1 ml	3 times

- Repeat PAS after nebs
- Prednisone (or equivalent) 2mg/kg orally with a maximum dose of 80 mg to any child with a PAS score over 7 after the first nebulizer treatment and not contraindicated.

Then follow algorithm





Treatment of acute severe asthma in PICU

1- monitoring:

Noninvasive blood pressure and oxygen saturations (SpO2). Those with respiratory failure requiring mechanical ventilation should undergo the placement of central venous, arterial, and urinary bladder catheters.

2- Oxygen:

Oxygen should be used as carrier gas for intermittent or continuous nebulization and to keep oxygen saturation above 92%.

3- Steroids

Methylprednisolone loading dose of 2 mg/kg followed by 0.5 to 1 mg/kg every 6 hours.

4- Bronchodilator

The usual dose for continuous albuterol nebulization ranges from 0.15 to 0.5 mg/kg/h.

Nebulized ipratropium, in 0.25 to 0.50 mg doses, can be used every 20 minutes during the first hour, followed by the same dose range every 6 hours.

5- Magnesium Sulfate

- The dose of magnesium sulfate is 25 to 50 mg/ kg/dose (maximum 2 g), infused for 20 to 30 minutes, and followed by continuous infusion dependent on the patient's weight.
- Children weighing < 30 kg: of 25 mg/kg/h
- Children weighing > 30 kg may receive 20 mg/kg/h,
- Infusion rates must not exceed 2 g/h in any patient. Titration to the desired clinical effect should be based on serum magnesium concentrations and tolerability.

Keep serum magnesium level below 6 mg /dl

- Observation of magnesium sulphate side effects:

Serum magnesium concentrations above 9 mg/dL causes:

- Nausea, flushing, somnolence, vision changes, muscle weakness and hypotension

Serum magnesium concentrations above 12 mg/dL causes:

- Respiratory depression and arrhythmias

6-Methylxanthines

- The theophylline dose is 80% of the aminophylline dose.
- A loading intravenous dose, 5mg/kg of theophylline or 6 mg/kg of aminophylline, given during 20 minutes is needed to achieve a therapeutic concentration.
- After the loading dose, a continuous infusion should be started. Infants younger than 6 months are 0.5 mg/kg/h
- Infants 6 months to 1 year 0.85 to 1 mg/kg/h
- Children 1 to 9 years, 1 mg/ kg/h
- Children older than 9 years, 0.75 mg/kg/h.

Serum drug concentrations should be obtained:

- 30 to 60 minutes after the loading dose is finished
- At 12 hours after the beginning of the continuous infusion
- Every 12 to 24 hours or when toxicity is suspected.

7-Mechanical ventilation of asthmatic patients:

- ***Bilevel Positive Airway Pressure***

Noninvasive positive pressure ventilation (NPPV) in addition to conventional therapy showed clinical improvement and correction of gas exchange abnormalities in children and adults with asthma. NPPV was well tolerated in children, including patients as young as 1 year

Typically recommended settings include an inspiratory positive airway pressure of 10 cm H2O, an expiratory positive airway pressure of 5 cm H2O, with or without a low back-up ventilation rate.

Criteria for selecting severe asthmatic patients for NPPV trial

- Tachypnea above normal limit of age
- Tachycardia above normal limit of age
- Use of accessory muscles of respiration
- Hypoxia with a Pa,O2/FI,O_2 ratio >200 mmHg
- Hypercapnia with Pa, CO_2, 60 mmHg FEV1< 50% pred"

Absolute and relative contraindication for noninvasive positive pressure ventilation (NPPV) trial

- **Absolute contraindications**
  - Need for immediate endotracheal intubation
  - Decreased level of consciousness
  - Excess respiratory secretions and risk of aspiration
  - Past facial surgery precluding mask fitting
- **Relative contraindication:**
  - Hemodynamic instability
  - Severe hypoxia and/or hypercapnia, Po2/Fio2 ratio of [200 mmHg, Pco2] 60 mmHg
  - Poor patient cooperation
  - Severe agitation
  - Lack of trained or experienced staff

- ***Invasive mechanical ventilation:***

1- Criteria for intubation

2- Recommendations for intubation technique

3- Recommendations for appropriate ventilator settings

4- Management in the immediate postintubation period

5- Medical management of asthma in the ventilated patient

6- Prevention and treatment of complications.

Step	Therapy	Comments
1	Albuterol, Ipratropium, Steroids	These medications should be ordered for all patients admitted to the PICU.
2	Continuous Albuterol	0.5-1 mg/kg/hr. If < 20 kg give 10-20 mg/hr; 20-30 kg give 10-30 mg/hr, > 30 kg give 15 -45 mg/hr
3	IV Magnesium	25 to 50 mg/kg/dose (max 2 g) infused over 20 to 30 min. Follow by continuous infusion of 15-25 mg/kg/hr. Mg level ≈ 4 mg/dL. Monitor for hypotension.
4	Heliox	Provide O_2 using non-rebreathing mask. May combine O_2 by nasal cannula if necessary to keep SaO_2 > 92%.
5	IV Terbutaline	Loading dose of 10 mcg/kg over 10 min followed by 0.4 mcg/kg/min. Increase by 0.4 mcg/kg/min every 15 min. Range 0.1 to 10 mcg/kg/min (average dose is 4 mcg/kg/min)
6	IV Theophylline	Loading dose of 5 mg/kg over 20 min followed by continuous infusion of 0.5-1 mg/kg/hr. Check serum theophylline concentration 30 min after the end of the loading dose. Target theophylline concentration is 10-20 mg/L
7	Non-Invasive Ventilation	Consider BiPAP to unload WOB. IPAP:10 EPAP:5
8	IV Ketamine	1 mg/kg/hr for sedation. Bronchodilatory properties. Increase airway secretions.
9	Intubation	Ketamine + Midazolam + Rocuronium
10	Ventilation	Try to avoid neuromuscular blockade. Permissive hypercapnia. PC/PRVC/PSV. Monitor peak to plateau pressure difference.

1- Criteria for Intubation:

- **Clinical:**
  -Cardiac arrest
  -Respiratory arrest
  -Progressive exhaustion

- Altered sensorium such as lethargy or agitation, interfering with oxygen delivery or anti-asthma therapy.

- **Laboratory:**

  -pH less than 7.2, carbon dioxide pressure increasing by more than 5 mm Hg/h or greater than 55 to 70 mm Hg, or oxygen pressure less than 60 mm Hg on 100% oxygen delivered through a mask.

  - Failure to reverse severe respiratory acidosis despite intensive therap.

2- Recommendation for intubation:

- ***Orotracheal intubation with sedation*** and neuromuscular blockade are preferred for asthmatic patients in critical respiratory distress.

- ***Intubation medication:***

  -Atropine at a dose of 0.02 mg/kg IV (minimum 0.1 mg, maximum 0.5 mg child, 1 mg adolescent) used to attenuate the vagal reflexes that lead to laryngospasm and worsen bronchospasm

  - Ketamine: 1.0 to 1.5 mg/kg I.V and 1.0 to 1.5 mg/kg succinylcholine I.V

  Ketamine: It stimulates the release of catecholamines leading to bronchodilation; Side effects include hypersecretion, hypotension and hypertension, arrhythmias, and hallucinations

  -Or propofol 2 mg/kg administered I.V over 2 minutes with succinylcholine, preferred in patients with hypertension, and succinylcholine should be avoided in patients with hyperkalemia.

3- Mechanical ventilation recommendations:

1) Low rate
2) Low PEEP
3) Prolonged expiratory time
4) Allow hypercapnia: till pH as low as 7.15 and a Pa CO2 of up to 80 mmHg

All these settings to avoid hyperinflation and auto-PEEP

5) Deal with expected complications:

- Hypotension:

☞ ***Look for:***

- Pneumothorax
- Hypovolemia
- High auto PEEP

- Cardiac arrest:

☞ ***Look for:***

- Hypoxia
- Exclude right mainstem intubation (21 cm at incisors)
- Exclude pneumothorax and place pleural drain
- Exclude pneumonia and other lung disease
- Pneumothorax

Mechanical ventilation algorithm

Atropine

Used to attenuate the vagal reflexes that lead to laryngospasm and worsen bronchospasm

(0.02 mg/kg IV minimum 0.1 mg, maximum 0.5 mg child, 1 mg adolescent)

↓

Ketamine

Stimulates the release of catecholamines leading to bronchodilation; Side effects include hypersecretion, hypotension and

(Dose: 1.0 to 1.5 mg/kg I.V)

↓

Intubation

(Orotracheal is preferable)

↓

Mechanical ventilation settings

Low rate

Low PEEP

Prolonged expiratory time

Allow hypercapnia

(Till pH as low as 7.15 and a Pa CO2 of up to 80 mmHg)

Refrences:

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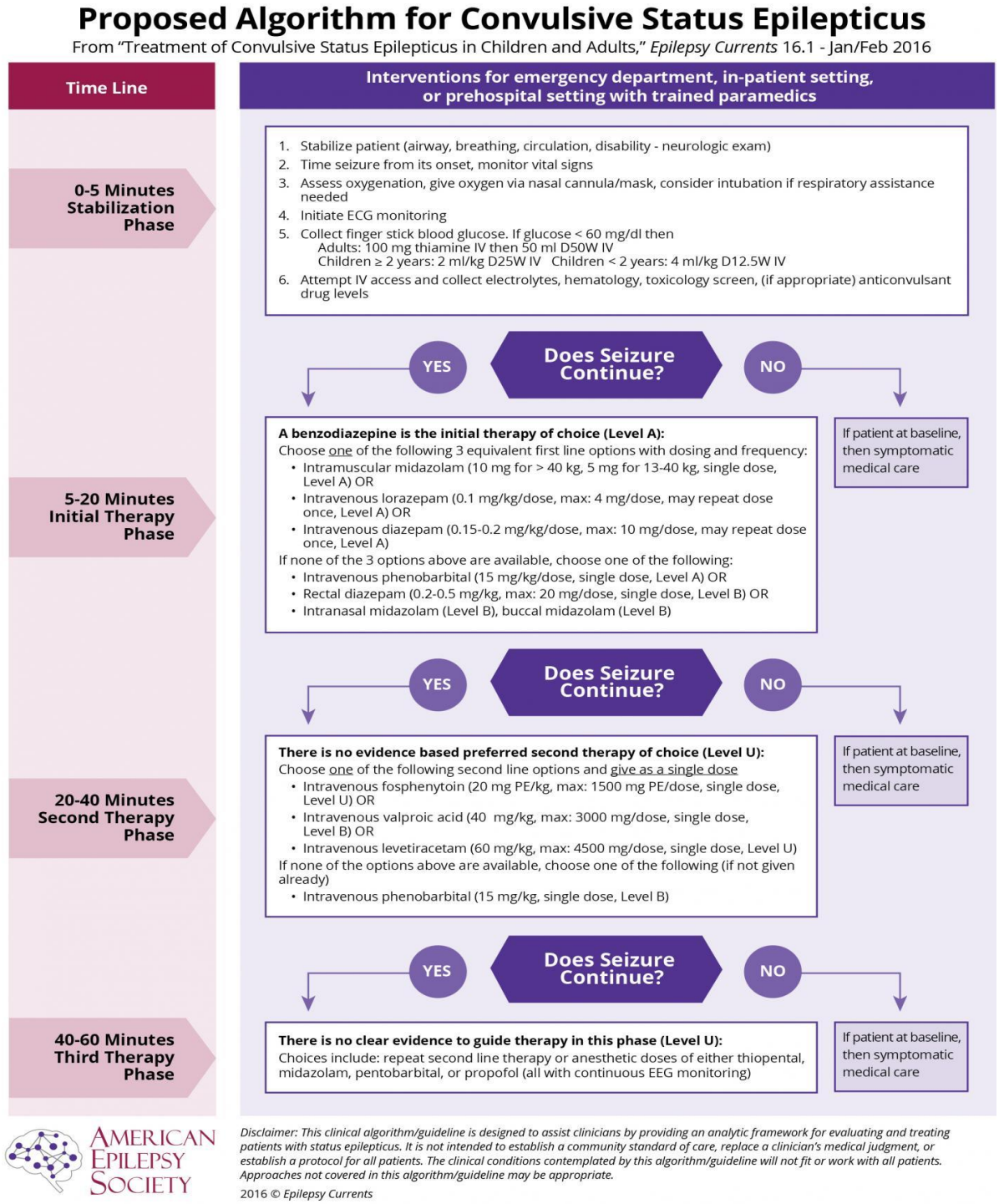
Status Epilepticus

Definition

5 min or more of (i) continuous clinical and/or electrographic seizure activity ***or*** (ii) recurrent seizure activity without recovery (returning to baseline) between seizures.



Intervention

Rapid sequence intubation

Midazolam continuous infusion

- IV 0.15 mg/kg bolus then 2 μg/kg/min
- Increase as needed by 2 μg/kg/min q5 minutes if still convulsing
- Bolus 0.15 mg/kg with each increase in infusion rate
- Maximum infusion rate 2 mg/kg/hr (34 μg/kg/min)
- Establish goals with guidance from specialist in neurology/critical care
- Maintain phenobarbital and phenytoin at therapeutic serum level (phenytoin goal level, 20-30 mg/mL; phenobarbital goal level, 40-50 mg/mL).

Do seizures persist?

Yes → Consider thiopental/ pentobarbital/ propofol bolus and continuous

No → If no seizures for 24-48 hours: Taper midazolam decrease by 1 μg/kg/min every 3 hours

Do seizures persist?

No → Taper drug if using continuous infusion

Yes → *Individualized therapy in consultation with neurology, critical care

*Consider add-on medications including levetiracetam, topiramate, ketamine, valproic acid, and ACTH ***or*** surgical options

Do seizures recur?

Yes → Reinstate midazolam for another 48 hours

No →

- Continue tapering midazolam
- Maintain phenobarbital and phenytoin within therapeutic serum level

Table (14): Intermittent drug dosing in SE *(Brophy et al., 2012)*

Drug	Initial dosing	Administration rates and alternative dosing recommendations	Serious adverse effects	Considerations
Diazepam	0.15 mg/kg IV up to 10 mg per dose, may repeat in 5 min	Up to 5 mg/min (IVP) Peds: 2–5 years, 0.5 mg/kg (PR); 6–11 years, 0.3 mg/kg (PR); greater than 12 years, 0.2 mg/kg (PR)	Hypotension Respiratory depression	Rapid redistribution (short duration), active metabolite, IV contains propylene glycol
Lorazepam	0.1 mg/kg IV up to 4 mg per dose, may repeat in 5–10 min	Up to 2 mg/min (IVP)	Hypotension Respiratory depression	Dilute 1:1 with saline IV contains propylene glycol
Midazolam	0.2 mg/kg IM up to maximum of 10 mg	Peds: 10 mg IM (>40 kg); 5 mg IM (13–40 kg); 0.2 mg/kg (intranasal); 0.5 mg/kg (buccal)	Respiratory depression Hypotension	Active metabolite, renal elimination, rapid redistribution (short duration)
Fosphenytoin	20 mg PE/kg IV, may give additional 5 mg/kg	Up to 150 mg PE/min; may give additional dose 10 min after loading infusion Peds: up to 3 mg/kg/min	Hypotension Arrhythmias	Compatible in saline, dextrose, and lactated ringers solutions
Lacosamide	200–400 mg IV	200 mg IV over 15 min No pediatric dosing established	PR prolongation Hypotension	Minimal drug interactions Limited experience in treatment of SE
Levetiracetam	1,000–3,000 mg IV Peds: 20–60 mg/kg IV	2–5 mg/kg/min IV		Minimal drug interactions Not hepatically metabolized
Phenobarbital	20 mg/kg IV, may give an additional 5–10 mg/kg	50–100 mg/min IV, may give additional dose 10 min after loading infusion	Hypotension Respiratory depression	IV contains propylene glycol
Phenytoin	20 mg/kg IV, may give an additional 5–10 mg/kg	Up to 50 mg/min IV; may give additional dose 10 min after loading infusion Peds: up to 1 mg/kg/min	Arrhythmias Hypotension Purple glove syndrome	Only compatible in saline IV contains propylene glycol
Topiramate	200–400 mg NG/PO	300–1,600 mg/day orally (divided 2–4 times daily) No pediatric dosing established	Metabolic acidosis	No IV formulation available
Valproate sodium	20–40 mg/kg IV, may give an additional 20 mg/kg	3–6 mg/kg/min, may give additional dose 10 min after loading infusion Peds: 1.5–3 mg/kg/min	Hyperammonemia Pancreatitis Thrombocytopenia Hepatotoxicity	Use with caution in patients with traumatic head injury; may be a preferred agent in patients with glioblastoma multiforme

IM intramuscular; *IV* intravenous; *IVP* intravenous push; *min* minute; *NG* nasogastric; *PE* phenytoin equivalents; *PEDs* pediatric; *PO* by mouth; *PR* rectal administration; *PRIS* propofol related infusion syndrome

Table (15): RSE dosing recommendations *(Brophy et al., 2012)*

Drug	Initial dose	Continuous infusion dosing recommendations-titrated to EEG	Serious adverse effects	Considerations
Midazolam	0.2 mg/kg; administer at an infusion rate of 2 mg/min	0.05–2 mg/kg/hr CI Breakthrough SE: 0.1–0.2 mg/kg bolus, increase CI rate by 0.05–0.1 mg/kg/hr every 3–4 h	Respiratory depression Hypotension	Tachyphylaxis occurs after prolonged use Active metabolite, renally eliminated, rapid redistribution (short duration), does NOT contain propylene glycol
Pentobarbital	5–15 mg/kg, may give additional 5–10 mg/kg; administer at an infusion rate ≤50 mg/min	0.5–5 mg/kg/h CI Breakthrough SE: 5 mg/kg bolus, increase CI rate by 0.5–1 mg/kg/h every 12 h	Hypotension Respiratory depression Cardiac depression Paralytic ileus At high doses, complete loss of neurological function	Requires mechanical ventilation IV contains propylene glycol
Propofol	Start at 20 mcg/kg/min, with 1–2 mg/kg loading dose	30–200 mcg/kg/min CI Use caution when administering high doses (>80 mcg/kg/min) for extended periods of time (i.e., >48 h) Peds: Use caution with doses >65 mcg/kg/min; contraindicated in young children Breakthrough SE: Increase CI rate by 5–10 mcg/kg/min every 5 min or 1 mg/kg bolus plus CI titration	Hypotension (especially with loading dose in critically ill patients) Respiratory depression Cardiac failure Rhabdomyolysis Metabolic acidosis Renal failure (PRIS)	Requires mechanical ventilation Must adjust daily caloric intake (1.1 kcal/ml)
Thiopental	2–7 mg/kg, administer at an infusion rate ≤50 mg/min	0.5–5 mg/kg/h CI Breakthrough SE: 1–2 mg/kg bolus, increase CI rate by 0.5–1 mg/kg/h every 12 h	Hypotension Respiratory depression Cardiac depression	Requires mechanical ventilation Metabolized to pentobarbital

CI continuous infusion; *EEG* electroencephalogram; *h* hour; *IM* intramuscular; *IV* intravenous; *IVP* intravenous push; *min* minute; *PRIS* propofol related infusion syndrome

N.B:

- **If patient is less than 18 months give pyridoxine 100 mg i.v**
- **As regards thiopental infusion:**
  - If thiopental infusion is started stop midazolam infusion
  - Increase thiopental infusion by 1mg/kg/hour every 30 min and give 2mg/kg bolus as needed if seizures is occurred on infusion
  - If convulsion is controlled Taper thiopental infusion after 24- 48 hours by 25% decrease every 12 hours
- **As regard propofol infusion:**
  - When seizures have been controlled for 12 hours, the drug dosage should be slowly reduced over a further 12 hours. If seizures recur, the drug infusion should be given again for another 12 hours, and then withdrawal attempted again. This cycle may need to be repeated every 24 hours until seizure control is achieved.
- **When to do EEG:**
  1. After clinical control of convulsion to diagnose subclinical status epilepticus
  2. After midazolam or thiopental or propofol infusion to document burst suppression

Acknowledgment:

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Ain Shams University
Pediatric Hospital

Pediatric ICU

PICU Protocols

Volume (2)

Diabetic ketoacidosis

Definition:

Diabetic Ketoacidosis is one of two serious, acute life-threatening complications of Type I diabetes mellitus (IDDM), or Type II, insulin insufficient diabetes mellitus, the other being severe hypoglycemia.

The biochemical criteria:

Blood glucose	> 200 mg/dL
Venous pH	< 7.3
bicarbonate	< 15 mmol/L
Ketonemia or Ketonuria	

The severity of DKA is categorized by the degree of acidosis

Degree	pH	HCO3
Mild	< 7.3	<15 mmol/L
Moderate	< 7.2	<10 mmol/L
severe	< 7.1	<5 mmol/L

Clinical signs:

1. Dehydration (which may be difficult to detect)
2. Tachycardia
3. Tachypnea (which may be mistaken for pneumonia or asthma)
4. Deep, sighing (Kussmaul) respiration; breath has the smell of acetone
5. Nausea, vomiting (which may be mistaken for gastroenteritis)
6. Abdominal pain that may mimic an acute abdominal condition
7. Confusion, drowsiness, progressive reduction in level of consciousness and, eventually, loss of consciousness.

Management:

Acute management should follow the general guidelines for PALS with particular attention to the following aspects for the child who presents in DKA.

1. Immediately measure BG and urine ketone concentrations with bedside meters.
2. Perform a clinical evaluation to identify a possible infection
3. Weigh the patient
4. Assess severity of dehydration:

5% dehydration	➢ Prolonged capillary refill time (normal capillary refill is ≤1.5–2 s) ➢ Abnormal skin turgor ('tenting' or inelastic skin) ➢ Abnormal respiratory pattern (hyperpnea). ➢ Dry mucus membranes, sunken eyes, absent tears, weak pulses, and cool extremities.
≥10% dehydration	➢ weak or impalpable peripheral pulses ➢ hypotension ➢ oliguria

5. Assess level of consciousness using Glasgow coma scale (GCS).
6. Additional measures is done of unconscious patient Secure the airway and empty the stomach by continuous nasogastric suction to prevent pulmonary aspiration
7. Give oxygen to patients with severe circulatory impairment or shock.
8. A cardiac monitor should be used for continuous electrocardiographic monitoring to assess T waves for evidence of hyper- or hypokalemia
9. Obtain a blood sample for laboratory measurement of:
    1. Serum or plasma glucose
    2. Electrolytes (including Na, K)
    3. Blood urea nitrogen, creatinine
    4. Serum osmolality

5. Venous pH, pCO2
6. Complete blood count. Note that an increased white blood cell count in response to stress is characteristic of DKA and is not indicative of infection.
7. Albumin, calcium, phosphorus, magnesium concentrations.
8. Urine analysis
9. Cultures (blood, urinary, sputum) only if evidence of infection
10. HbA1c to assess duration of hyperglycemia
11. ECG is done if serum measurement of K is delayed

10. Give antibiotics to febrile patients after obtaining appropriate cultures of body fluids
11. Catheterization of the bladder usually is not necessary, but if the child is unconscious or unable to void on demand (e.g., infants and very ill young children) the bladder should be catheterized

☒ ***Goals of therapy***:

a. Correct dehydration
b. Correct acidosis and reverse ketosis
c. Restore BG to near normal
d. Monitor for complications of DKA and its treatment
e. Identify and treat any precipitating event

☒ **Calculations:**

❖ Anion gap = Na − (Cl + HCO3): normal is 12 ± 2 mmol/L.
- In DKA, the anion gap is typically 20–30 mmol/L; an anion gap >35 mmol/L suggests concomitant lactic acidosis.

❖ Corrected sodium = measured Na + 2 [(plasma glucose − 100)/100] mg/dL.

✓ Patients with DKA are liable for hyponatremia due to:
- Glucose largely restricted to the extracellular space, causes osmotic movement of water into the extracellular space thereby causing dilutional hyponatremia
- the low sodium content of the elevated lipid fraction of the serum in DKA

1-Fluid therapy:

Fluid replacement should begin before starting insulin therapy.

1. ***Antishock therapy***:

   It is given as required, to restore peripheral circulation.

   - Patients not in shock but with volume depletion ⟶ 10: 20 ml /kg over 1: 2 hours may need to be repeated until tissue perfusion is adequate.
   - Patient with DKA in shock: rapidly restore circulatory volume with isotonic saline in 20 mL/kg boluses infused as quickly as possible through a large bore cannula with reassessment after each bolus.

2. ***Deficit therapy:***

   - In moderate DKA 5- 7% (50:70 ml/ kg)
   - In sever DKA 7-10% (70:100 ml/kg)

Calculate the subsequent rate of fluid administration, including the provision of maintenance fluid requirements, aiming to replace the estimated fluid deficit evenly over 48 h.

Maintenance fluid: to be calculated based on body weight.

100cc/kg for the first 10kg, 50cc/kg for the next 10kg, and 20 cc/kg thereafter

The rate of fluid administration should seldom exceed 1.5–2 times the usual daily maintenance requirement.

Body weight, kg	Maintenance mL/24 hr	DKA: give maintenance+ 5% of body weight/24 hr	
		mL/24hr	mL/hr
4	325	530	22
5	405	650	27
6	485	790	33
7	570	920	38
8	640	1040	43
9	710	1160	48
10	780	1280	53
11	840	1390	58
12	890	1490	62
13	940	1590	66
14	990	1690	70
15	1030	1780	74
16	1070	1870	78
17	1120	1970	82
18	1150	2050	85
19	1190	2140	89
20	1230	2230	93
22	1300	2400	100
24	1360	2560	107
26	1430	2730	114
28	1490	2890	120
30	1560	3060	128
32	1620	3220	134
34	1680	3360	140
36	1730	3460	144
38	1790	3580	149
40	1850	3700	154
45	1980	3960	165
50	2100	4200	175
55	2210	4420	184
60	2320	4640	193
65	2410	4820	201
70	2500	5000	208
75	2590	5180	216
80	2690	5380	224

Table 1: showing maintenance volumes, also after subtraction of initial boluses given for the patient assuming it was 10-20 ml/ kg

Duration of IV fluid therapy:

Divide fluids over remainder of time for replacement: This is calculated based on serum osmolality (mosmol/kg H_2O):

$$\text{Calculate s-osmolality} = Na^{+}_{(meq/l)} \times 2 + \frac{\text{glucose (mg / dl)}}{18} + \frac{\text{BUN (mg / dl}}{2.8}$$

- If **s-osmolality 300 - ≤ 320** → correct **over 24 hours**
- If **s-osmolality > 320 - < 340** → correct **over 36 hours.**
- If **s-osmolality ≥ 340 or initial sNa^{+}>150 meq/L** → correct **over 48hours.**

2. Insulin therapy:

Insulin therapy: begin with 0.1 U/kg/h in patients above five years

0.05 U/Kg/h in patients below five years

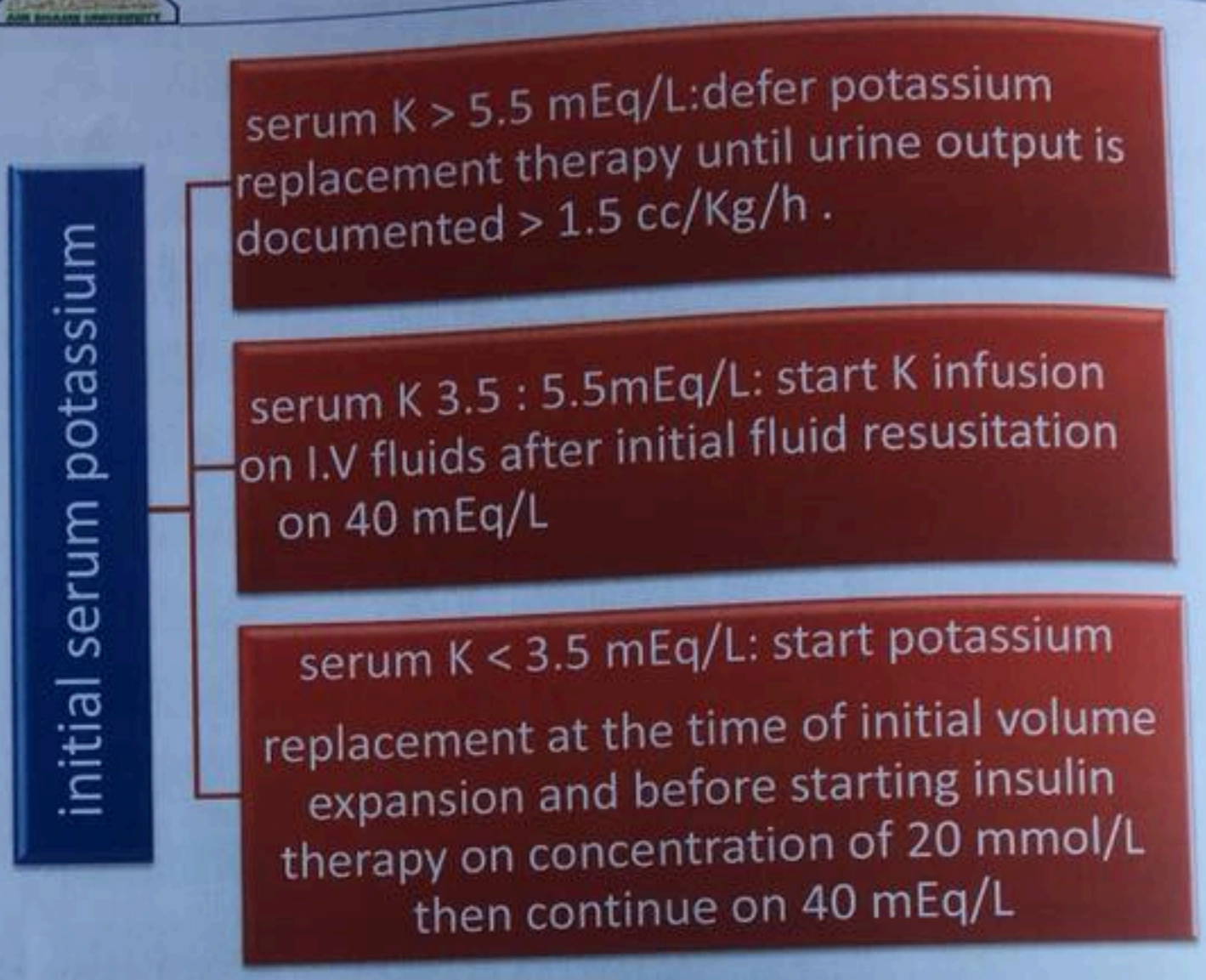
Insulin drip start 1–2 h AFTER starting fluid replacement therapy.

Dilute 50 units regular human insulin in 500 mL normal saline, (0.1 unit insulin =1 mL).

3. Potassium replacement:

If immediate serum potassium measurements are unavailable, an ECG may help to determine whether the child has hyper- or hypokalemia.

Signs of hypokalemia in ECG:	➢ Prolongation of the PR interval ➢ T-wave flattening and inversion ➢ ST depression, prominent U waves ➢ apparent long QT interval (due to fusion of the T and U waves)
Signs of hyperkalemia in ECG:	➢ Tall, peaked, and symmetrical T waves ➢ shortening of the QT interval



4. Bicarbonate administration:

Bicarbonate administration is not recommended except for treatment of life-threatening hyperkalemia.

Bicarbonate is NOT recommended and has potential hazards in patients with DKA:

1. HCO_3 diffuses slowly through BBB

   $(HCO_3 + H^+ \rightarrow CO_2 + H_2O)$

CO_2 diffuses rapidly → paradoxical CNS acidosis * ↑ risk of cerebral edema.

2. Alkalosis is associated with hypokalemia.
3. May ↑ s-Na^+ in a patient with hyperosmolar dehydration.
4. HCO_3^- therapy shifts the OxyHb dissociation curve to the left (decreases O_2 release to the tissues) → ↑ tissue hypoxia.

Indication for bicarbonate therapy in patients with DKA:

(1) A patient with pH < 6.9 who is in shock with decreased cardiac contractility and peripheral vasodilatation with poor tissue perfusion.

(2) Patients with LIFE THREATENING Hyperkalemia.

- In these cases only Give $NaHCO_3$ 1-2 meq/kg or 80 meq/m^2 body surface area added to 0.45% saline over 1 hour (never by bolus).
- Be careful about s-K^+ and DO NOT stop K^+ infusion while bicarbonate is being given.
- Reassess after 1 hour of finishing bicarbonate infusion.

Rate of I.V fluid administration:

Rate of I.V fluid and insulin drips depend on RBS and rate of decent of RBS/ Hour which should not exceed 90 mg/dL.

RBS level	Type of I.V fluid	Rate of insulin drip
> 300 mg/dL	Saline 0.9 %	➢ > 5 years 0.1 IU/kg/h ➢ > 5 years 0.05 IU/kg/h
140 :300 mg/dL Or rate of decrease > 90 mg/dL	Saline 0.9%: glu 5%	Same rate
80: 140 mg/dL Or rate of decrease > 90 mg/dL	Saline 0.9%: glu 10%	Same rate
> 80 mg/dL Or rate of decrease > 90 mg/dL	Saline 0.9%: glu 12.5%	Same rate
> 80 mg/dL Or rate of decrease > 90 mg/dL	Saline 0.9%: glu 12.5%	Decrease to half rate

If rate of blood sugar decrease less than 30 mg/dL or acidosis is not corrected so you should revaluate:

1. IV fluid calculations
2. Insulin delivery system & dose
3. Need for additional resuscitation
4. Consider sepsis

☒ *Clinical and biochemical monitoring*

There should be documentation on a flow chart of hour-by-hour clinical observations, IV and oral medications, fluids, and laboratory results. Monitoring should include the following:

• Hourly (or more frequently as indicated) vital signs (heart rate, respiratory rate, blood pressure).

• Hourly (or more frequently as indicated) neurological observations (GCS) for warning signs and symptoms of cerebral edema that include:

1) Headache
2) Inappropriate slowing of heart rate
3) Recurrence of vomiting
4) Change in neurological status (restlessness, irritability, increased drowsiness, incontinence)
5) Specific neurologic signs (e.g., cranial nerve palsies, abnormal pupillary responses)
6) Rising blood pressure
7) Decreased oxygen saturation
8) Rapidly increasing serum sodium concentration suggesting loss of urinary free water as a manifestation of diabetes insipidus (from interruption of blood flow to the pituitary gland due to cerebral herniation)

9) Failure of measured serum sodium levels to rise or a further decline in serum sodium levels with therapy is thought to be a potentially ominous sign of impending cerebral edema. Too rapid and ongoing rise in serum sodium concentration may also indicate possible cerebral edema as a result of loss of free water in the urine from diabetes insipidus.

- Amount of administered insulin.
- Hourly (or more frequently as indicated) accurate fluid input (including all oral fluid) and output.
- Capillary blood glucose concentration should be measured hourly (but must be cross-checked against laboratory venous glucose, as capillary methods may be inaccurate in the presence of poor peripheral circulation and acidosis).
- Laboratory tests: serum electrolytes, glucose, blood urea nitrogen, calcium, magnesium, phosphorus, hematocrit, and blood gases should be repeated 2–4 h, or more frequently, as clinically indicated, in more severe cases.

Where Should the Patient be treated ? Indications for ICU admission:

1. Patients with severe DKA: (pH < 7.1, shock, or with long duration of symptoms).
2. Patients with altered level of consciousness.
3. DKA in children below 5 years (are at increased risk of cerebral edema).
4. Patients with high BUN, possible oliguria & acute tubular necrosis (for need of a central venous catheter & dialysis).
5. If cerebral edema develops as a complication of treatment.

Introduction of oral fluids and shift to S.C. insulin

- Can introduce oral fluids after substantial clinical improvement (mild acidosis/ketosis may still be present).
- Plan to change to SC insulin when ketoacidosis has resolved (pH > 7.3 , HCO_3 > 15, anion gap is normal) + oral fluids are tolerated.

- Best is to shift before a meal time.
- Start S.C. intermediate acting + short acting insulin.

To prevent rebound hyperglycemia, the first SC injection should be given 15–30 min (with rapid acting insulin) or 1–2 h (with regular insulin) before stopping the insulin infusion to allow sufficient time for the insulin to be absorbed. With intermediate or long-acting insulin, the overlap should be longer and the rate of IV insulin infusion gradually lowered.

Introduction of oral fluids and shift to S.C. insulin

- Can introduce oral fluids after substantial clinical improvement (mild acidosis/ketosis may still be present).
- Plan to change to SC insulin when ketoacidosis has resolved (pH > 7.3 , HCO_3 > 15, anion gap is normal) + oral fluids are tolerated.
- Best is to shift before a meal time.

Start S.C. intermediate acting + short acting insulin.

- ***Calculate insulin dose as :***

0.7 U/kg/d in prepubertal children with long standing DM (may need IU/kg/d in new cases).

1.0 U/kg/d at midpuberty.

1.2 U/kg/d by the end of puberty.

- Give the first dose of rapid-acting insulin analogue 15 minutes before stopping insulin infusion and of regular insulin 1 hour before stopping it.

Cerebral edema:

The incidence of clinically overt cerebral edema in national population studies is 0.5–0.9% and the mortality rate is 21–24%

Diagnosis is established by:

1. One diagnostic criterion ***or***
2. two major criteria ***or***
3. one major and two minor criteria

These have a sensitivity of 92% and a false positive rate of only 4%. Signs that occur before treatment should not be considered in the diagnosis of cerebral edema.

Diagnostic criteria	*Major criteria*	*Minor criteria*
• Abnormal motor or verbal response to pain • Decorticate or decerebrate posture • Cranial nerve palsy (especially III, IV, and VI) • Abnormal neurogenic respiratory pattern (e.g., grunting, tachypnea, Cheyne–Stokes respiration, apneusis)	• Altered mentation/fluctuating level of consciousness • Sustained heart rate deceleration (decrease more than 20 beats/min) not attributable to improved intravascular volume or sleep state • Age-inappropriate incontinence	• Vomiting • Headache • Lethargy or not easily arousable • Diastolic blood pressure >90mmHg • Age <5 yr

Treatment of cerebral edema:

Initiate treatment as soon as the condition is suspected.

i. Reduce the rate of fluid administration by one-third.
ii. Give mannitol, 0.5–1 g/kg IV over 10–15 min, and repeat if there is no initial response in 30 min to 2 h.
iii. Hypertonic saline (3%), suggested dose 2.5–5 mL/kg over 10–15 min, may be used as an alternative to mannitol, especially if there is no initial response to mannitol
iv. Hyperosmolar agents should be readily available at the bedside.
v. Elevate the head of the bed to 30.◦
vi. Intubation may be necessary for the patient with impending respiratory failure.
vii. After treatment for cerebral edema has been started cranial imaging may be considered as with any critically ill patient with encephalopathy or acute focal neurologic deficit. The primary concern is whether the patient has a lesion requiring emergency neurosurgery (e.g., intracranial hemorrhage) or a lesion that may necessitate anticoagulation (e.g cerebrovascular thrombosis)

References:

- ISPAD Clinical Practice Consensus Guidelines 2014 Compendium
- Protocol of Management of Type 1 Diabetes Mellitus, the Diabetes Clinic Children's Hospital - Ain Shams University

Immediate assessment

Clinical History
Polyuria
Polydipsia
Weight loss (Weigh)
Abdominal pain
Tiredness
Vomiting
Confusion

Clinical Signs
Assess dehydration
Deep sighing respiration (Kussmaul)
Smell of ketones
Lethargy/drowsiness ± vomiting

Biochemical features & investigations
Ketones in urine
Elevated blood glucose
Acidemia
Blood gases, urea, electrolytes
Other investigations as indicated

Diagnosis confirmed
Diabetic Ketoacidosis
Contact Senior Staff

Shock (reduced peripheral pulses)
Reduced conscious level/coma

Dehydration >5%
Not in shock
Acidotic (hyperventilation)
Vomiting

Minimal dehydration
Tolerating oral fluid

Resuscitation
Airway ± NG tube
Breathing (100% oxygen)
Circulation (0.9% saline 10-20 ml/kg over 1-2 h. & repeat until circulation is restored) but do not exceed 30 ml/kg

IV Therapy
Calculate fluid requirements
Correct over 48 hours
Saline 0.9%
ECG for abnormal T-waves
Add K 40 mmol/L fluid

Therapy
Start with SC insulin
Continue oral hydration

No improvement

Continuous insulin infusion started 1-2 hours after fluids (0.05-.1 unit/kg/hour)

Critical Observations
Hourly blood glucose
Hourly fluid input & output
Neurological status at least hourly
Electrolytes 2 hourly after start of IV therapy
Monitor ECG for T-wave changes

Acidosis not improving deterioration

Re-evaluate
IV fluid calculations
Insulin delivery system & dose
Need for additional resuscitation
Consider sepsis

Blood glucose ≤17 mmol/l (300mg/dL)
or
blood glucose falls >5 mmol/l/hour (90 mg/dL)

IV Therapy
Change to 0.45% saline + 5% glucose
Adjust sodium infusion to promote an increase in measured serum sodium

Improvement
Clinically well, tolerating oral fluids

Transition to SC Insulin
Start SC insulin **then** stop IV insulin after an appropriate interval

Neurological

WARNING SIGNS:
headache, slowing heart rate, irritability, decreased conscious level, incontinence, specific neurological signs

Exclude hypoglycaemia
Is it cerebral edema?

Management
Give mannitol 0.5-1 g/kg or hypertonic saline
Restrict IV fluids by one-third
Call senior staff
Move to ICU
Consider cranial imaging **only** after patient stabilised

Stress hyperglycemia

Hyperglycemia is common in acute illness, even in the absence of known prior insulin resistance or diabetes mellitus (DM). Stress hyperglycemia is common in pediatric critical illness, with an estimated 49–72% of children experiencing BG concentrations >150 mg/dl

Effect:

1. Several studies have demonstrated the association of stress hyperglycemia in critically ill children with mortality
2. Stress hyperglycemia is associated with longer periods of ICU and hospital stay and more frequent nosocomial infections, including surgical site infections in critically ill children
3. Poor clinical outcome

Causes:

1. Elevated levels of ant insulin hormones as: cortisol, glucagon, growth hormone, catecholamines, and various cytokines, which stimulate glycogenolysis and gluconeogenesis, resulting in a transient increase in blood glucose concentration that typically normalizes when the stress abates.
2. Relative insulin deficiency, peripheral insulin resistance, and dehydration causing decreased renal perfusion with limitation of urinary glucose excretion

Management:

Different protocols are adapted for management of stress hyperglycemia in different institutes

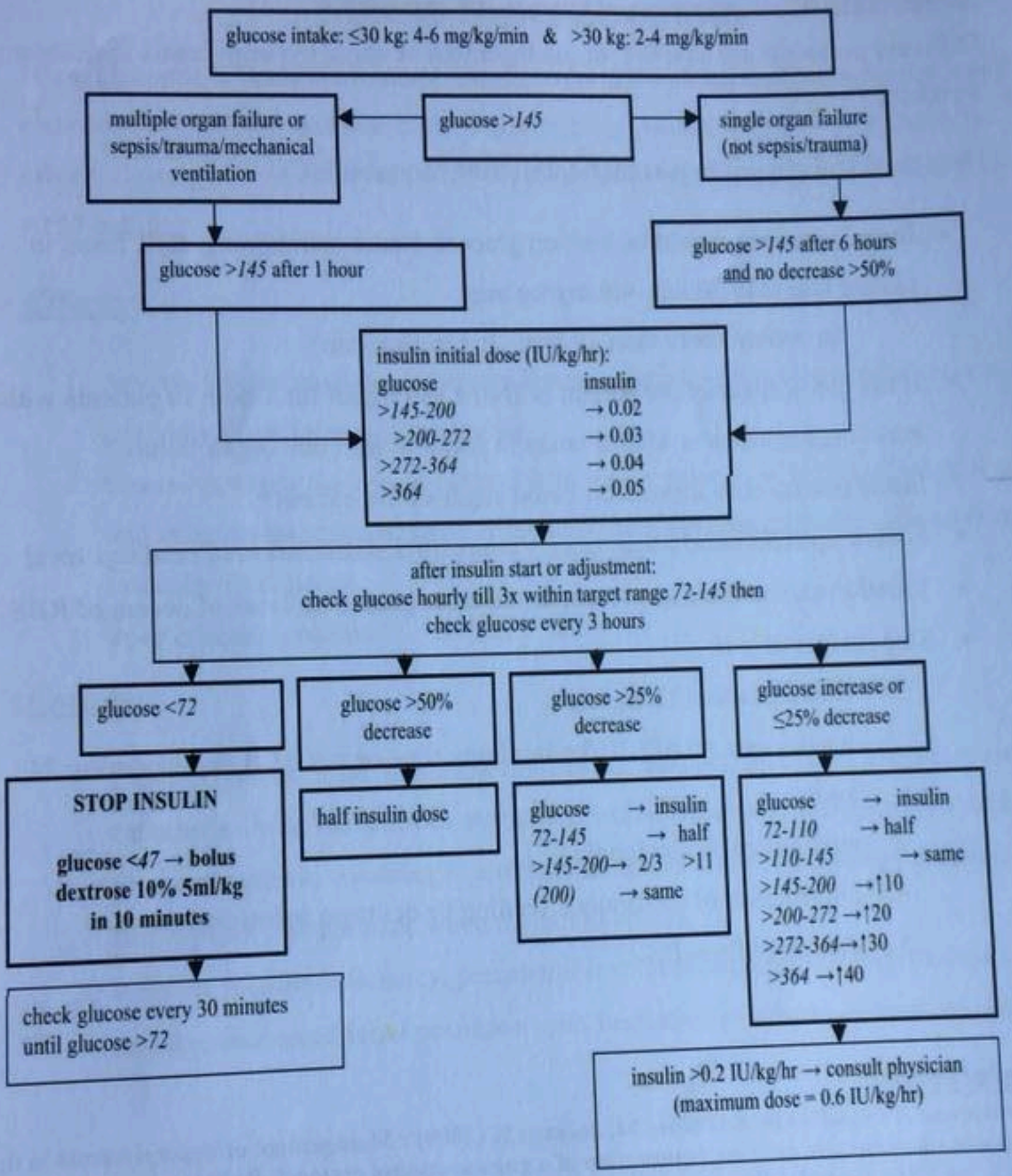
Here the protocol used in Ain shams university hospital PICU

- Initially patient should be kept on glucose intake maintaining GIR from: in patient less than 30 kgs 4:6 mg/kg/min

  In patient more than 30 kgs 2: 4 mg/kg/min
- If the blood sugar of the patient is above 150 mg/dl for 1 hour in patients with multi organ failure or after 6 hours in patients with one organ failure
- Initial insulin dose depend on blood sugar of the patient
- Follow up RBS hourly than after 3 hours after stabilization of readings level
- Titration can be done as present in the table guided by level of decent of RBS
- Stop insulin drip if:
  1. -blood glucose 72 mg/dL
  2. -insulin rate <0.015 IU/kg/hr at any time or < 0.03 IU/kg/hr during 24 hours
  3. -start enteral bolus feeding
  4. -interruption of continuous feeding or dextrose infusions
  5. -discharge from PICU

References:

Verhoeven J, Brand J,van de Polder M, Joosten K (2009) : Management of hyperglycemia in the pediatric intensive care unit; implementation of a glucose control protocol, Pediatric Critical Care Medicine 2009; 10: 648-652.



Stop criteria:

-blood glucose <72 mg/dL

-insulin rate <**0.015** IU/kg/hr at any time or < **0.03** IU/kg/hr during 24 hours -start enteral bolus feeding

-interruption of continuous feeding or dextrose infusions

-discharge from PICU\

Acute adrenal insufficiency

Definition:

Adrenal insufficiency is defined by the impaired synthesis and release of adrenocortical hormones.

It is classified based upon the mechanism:

A. Primary adrenal insufficiency, also known as Addison's disease, results from disease intrinsic to the adrenal cortex.

B. Central adrenal insufficiency is caused by impaired production or action of adrenocorticotropic hormone (ACTH). It can be caused by several mechanisms:

1. Secondary adrenal insufficiency results from pituitary disease impairing release of adrenocorticotropic hormone (ACTH). In addition, unresponsiveness of end-organs to adrenocortical hormones is classified as secondary adrenal insufficiency because this presents in a similar manner as diseases caused by adrenocorticotropic hormone (ACTH) deficiencies.

2. Tertiary adrenal insufficiency results from the impaired release or effect of corticotropin releasing hormone (CRH) from the hypothalamus.

Causes:

Major Causes are listed in the table below

Primary adrenal insufficiency	Secondary adrenal insufficiency	Tertiary adrenal insufficiency
Steroidogenesis disorders • Congenital adrenal hyperplasia • Defects in aldosterone production • Wolman disease • Smith-Lemli-Opitz syndrome	**Pituitary etiology** Congenital: • PROP-1 gene mutation • Pit-1 gene mutation • Idiopathic isolated ACTH deficiency Acquired: • Brain tumor • Brain hemorrhage • Brain surgery Cranial radiation	**Isolated ACTH deficiency** • CRH gene defect • CRH receptor defect **Congenital malformations of the brain** Septo-optic dysplasia
Damage to otherwise normal adrenal glands • Bilateral adrenal hemorrhage of the newborn • Adrenal hemorrhage of acute infection • Kearns-Sayre syndrome • Polyglandular autoimmune syndromes • Infection as TB, HIV, CMV • Drugs as Ketoconazole	**End organ unresponsiveness** • Familial glucocorticoid resistance • Pseudohypoaldosteronism 1	**Temporary isolated ACTH deficiency due to suppression of hypothalamic CRH secretion** • Cessation of pharmacologic glucocorticoid therapy • Megestrol acetate (Megace) therapy • Resection of a unilateral cortisol-secreting tumor • Resection of an ACTH-secreting tumor • Infants born to steroid treated mothers
Peroxisomal defects • X-linked Adrenoleukodystrophy • Refsum disease • Zellweger syndrome		**Brain injury** • Brain tumor • Brain hemorrhage • Brain surgery Cranial radiation
Unresponsive to ACTH • Familial glucocorticoid deficiency • Triple A syndrome (Allgrove syndrome)		**Infiltrative diseases (also cause secondary adrenal insufficiency)** • Hemochromatosis • Sarcoidosis • Langerhans cell histiocytosis

Clinical picture:

In neonates it can be presented with ambiguous genitalia in some types of congenital adrenal hyperplasia

Glucocorticoid deficiency	Mineralocorticoid deficiency	Adrenal androgen deficiency in females	Increased melanocortin production
• Gastrointestinal symptoms (nausea, vomiting) • Fatigue, weakness • Failure to thrive • Morning headache • Fasting hypoglycemia • Increased insulin sensitivity • Decreased gastric acidity • Decreased free water clearance	• Hypotension, dizziness • Muscle weakness • Fatigue • Gastrointestinal symptoms (nausea, vomiting, anorexia) • Salt-craving • Weight loss • Dehydration • Hyponatremia, hyperkalemia, metabolic acidosis, hypoglycemia	• Decreased pubic and axillary hair development in pubertal patients • Decreased libido in older patients	• Hyperpigmentation of skin, mucosa, palmar creases, axillae, gingival borders

Investigation:

- Electrolytes: hyponatremia and hyperkalemia
- ABG: metabolic acidosis
- Hypoglycemia
- 17 OH Progesterone
- Serum cortisol 8 am
- ACTH stimulation test

When to suspect adrenal crisis:

•Hypotension or shock, particularly if disproportionate to apparent underlying illness.

•Serum electrolyte abnormalities:

A. Hyponatremia with or without hyperkalemia

B. Metabolic acidosis

C. Hypoglycemia

•Vomiting and diarrhea, sometimes with severe abdominal pain or unexplained fever, weight loss and anorexia.

Consider the diagnosis in:

1. Any patient with known disorders of adrenal insufficiency (eg, congenital adrenal hyperplasia), especially if exposed to stress (illness.(
2. Other patients presenting with the above signs, especially with hyperpigmentation or vitiligo.
3. Critically ill patients with septic shock, who are unresponsive to fluid resuscitation and inotropic medications (in this case, adrenal crisis can be caused by bilateral adrenal hemorrhage).
4. Patients on or withdrawing from chronic treatment with corticosteroids, especially if exposed to stress.
5. Patients with other autoimmune endocrine deficiencies, such as type 1 diabetes mellitus, hypothyroidism, or gonadal failure.

In neonates:

•Neonates with the above symptoms and signs should prompt consideration of the diagnosis of congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency, or (very rarely) other causes of adrenal insufficiency

- Adrenal crisis usually presents between the first and fourth week of life. Affected females will have ambiguous genitalia; males usually have no obvious genital abnormalities.
- The presentation of adrenal crisis in an infant may mimic that of pyloric stenosis. However, infants with pyloric stenosis typically have hypokalemic alkalosis rather than the hyperkalemic acidosis that is typical of adrenal crisis.

Evaluation:

•If adrenal crisis is suspected, then patients should be treated empirically with stress doses of corticosteroids, as outlined below.

•Baseline blood samples should be drawn for subsequent testing for electrolytes, glucose, cortisol and other adrenal steroids, ACTH, and renin, prior to the administration of corticosteroids. Treatment should not be delayed pending results.

Treatment:

1. *Intravenous fluids*

Fluid requirements:

Maintenance = 100ml/kg/day for first 10kg body weight, 50ml/kg/day for next 10kg, 25ml/kg/day for each successive 10kg

Deficit = 100ml/kg for 10% dehydration, 60 ml/kg for 6% dehydration and 30ml/kg for 3% dehydration.

Shock or severe dehydration:

1. Give **isotonic saline (0.9% saline) bolus at 10-20ml/kg** during the first hour of treatment. This may be repeated until circulation is restored.
2. Replace remaining deficit + maintenance fluid requirements evenly over 24 hours. Commence this rehydration with **Plasma-Lyte 148 (or Ringer solution) and 5% Glucose**. If potassium is high, use **0.9% saline and 5% glucose**.

3. Check pH, electrolytes and glucose frequently

    - Blood gases and RBS hourly x 2 hours; then 2-4 hourly once normoglycaemic and acidosis correcting.
    - Electrolytes: 2 hourly initially (more frequently if significant hyperkalemia - see below)
    - Interval can then be extended once glucose stable and electrolytes normalizing.

4. Avoid rapid rise in serum sodium.

Moderate dehydration:

- Normal saline 10 ml/kg i.v. bolus. Repeat until circulation is restored.
- Administer remaining deficit plus maintenance fluid volume as Plasma-Lyte 148(or Ringer solution) and 5% Glucose (unless hyperkalaemic) evenly over 24 hours.
- Check blood gas, electrolytes and glucose frequently as above

Mild or no dehydration:

- No bolus.
- 1-1.5 times maintenance fluid volume as Plasma-Lyte 148(or Ringer solution) and 5% Glucose (unless hyperkalaemic) administered evenly over 24 hours.
- Check electrolytes and glucose frequently as above / clinically indicated

* Note: 10% dextrose may be required to maintain normoglycaemia

2. *Steroid replacement*

1. Give IV bolus of hydrocortisone hemisuccinate (Solu-Cortef) immediately (dose for age as shown below). If IV access is not immediately available, give IM while establishing intravenous access
2. Follow with hydrocortisone 6hourly IV.

Neonate – 6 weeks	**25 mg I.V and then 5-10 mg every 6 hours**
6 weeks up to 3 years	25 mg I.V initial dose then 1 mg every 6 hours
Children 3 to 12 years	50 mg IV initial dose then 12.5 from 3 :6 years and 25 mg from 6: 12 years every 6 hours
Children and adolescents	12 years and older: 100 mg IV then 25 mg every 6 hours

- Alternatively, the dose may be based upon body surface area (50 to 100 mg/m2)

3. *Electrolytes:*

- If hyperkalemia is present, perform ECG to evaluate: initially a tall peaked T wave with shortened QT interval, followed by progressive lengthening of the PR interval and QRS duration.
- If these changes are present, treat with insulin and glucose infusion, with or without other measures to treat hyperkalemia (See part 1)

4. Switch to oral steroid therapy:

- When child is stable, reduce the IV dose, or if tolerating oral meds switch to triple dose oral hydrocortisone replacement (~30-50mg/m2/day).
- This can then be gradually reduced to maintenance levels (10-15 mg/m2/day in primary adrenal insufficiency, or 6-8 mg/m2/day in secondary adrenal insufficiency) over about 5 days. Endocrinology team will advise on dosing schedule.
- Mineralocorticoid replacement: in patients with mineralocorticoid deficiency start fludrocortisone at maintenance doses (usually 0.05 - 0.1 mg daily) as soon as patient can tolerate oral fluids.
- NB. Prednisolone has little / no mineralocorticoid activity

References:

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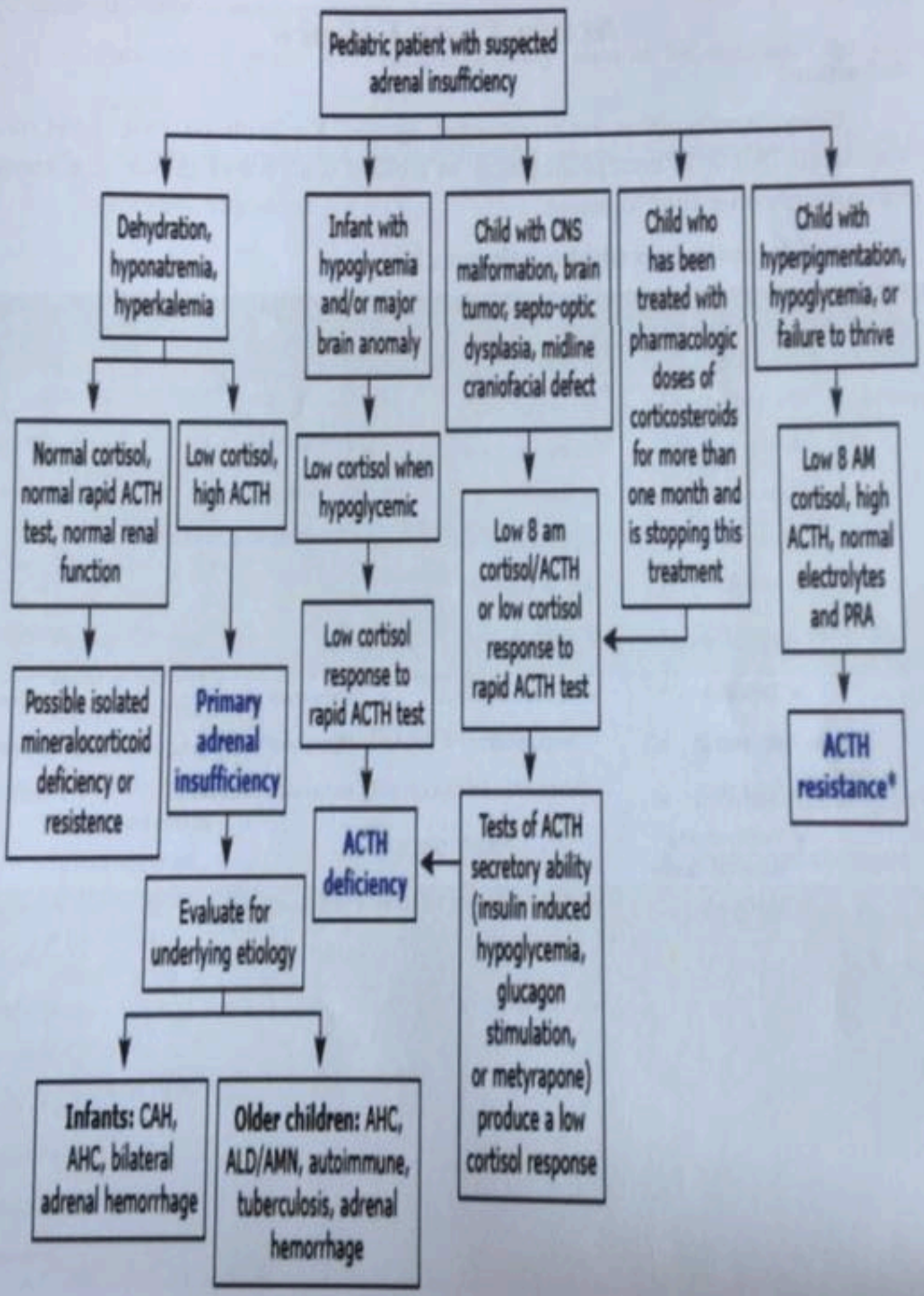

Acute Liver Failure

Definition:

Coagulopathy (that isn't corrected by vit. K) With (if INR 1.5-1.9) or without (if INR > 2) encephalopathy in a child with no evidence of a known previous chronic liver disease.

Stages of hepatic encephalopathy:

Stages / Cl/P	I	II	III	IV
Symptoms	Periods of lethargy, euphoria, reversal of day-night sleeping; may be alert	Drowsiness, inappropriate behavior, agitation, wide mood swings, disorientation	• Stupor but arousable. • Confused, incoherent speech	• Coma • Iva: responds to noxious stimuli • IVb: no response.
Signs	• Trouble drawing figures, • Performing mental tasks	• Asterixis, fetor hepaticus, incontinence	• Asterixis, rigidity, hyperreflexia, extensor reflexes.	• Areflexia, no asterixis, flaccidity.
EEG	• Normal	• Generalized slowing, • q Waves.	• Markedly abnormal, triphasic wave.	• Markedly abnormal, bilateral slowing , d waves, electric cortical silence.

General lines of management:

- Patients in grade 1-2 encephalopathy should be managed in hospital (ward).
- Patients in grade 3-4 encephalopathy should be managed in PICU and probably intubated.

Management

1. History

2. Past history Drugs

3. History of :

1.Causes :

- HAV, HBV, HCV.
- EBV, CMV, HSV
- HLH.
- Heart failure (shock liver) pancreatitis.
- Autoimmune ds
- If infant: Galactosemia
- Tyrosinemia, Mitochondrial ds and UCD.
- Wilson's ds
- Sepsis, shock, MOF
- Cerebral edema.

- Acetaminophen (most common cause)
- Halothane
- Isoniazid.
- Na valproate.
- Herbal supplements.
- Mushroom

- Neurodevelopmental delay.
- School problems.
- Lethargy.
- Sleep reversal
- Intellectual impairment
- Personal changes.
- Writing deterioration

II O/E

(1)General:

Vital data
* RBS
* Temp. *wt daily
* HR, RR *Bpr
* CRT
* GCS

(2) Local

Other systems:
Abdomen Neuro *Chest&cardiac

Ascites organomegly

* ↑ tendon
*Flapping tremors
*Pupils

III. Investigations

1. Laboratory

For disease:

- CBC with retics
- PT, PTT, INR
- Liver profile
- s. Albumin
- Renal profile
- Na, K, Po_4, Mg
- NH_3
- S. lactate and Pyruvate
- ABG

For causes:

- Cultures
- Viral marker
  a. HAV IgM, HBsAg, HBcAb IgM, HCV, Ab
  b. Serologic & PCR for HSV, CMV, EBV
- Toxicological screen, e.g. Acetaminophen level, valproate level.
- Amylase.
- Autoantibody Igs.
- Ceruloplasmin.
- Metabolic screen (infant).
- HLH markers (s.ferritin, fibrinogen, TAG)

2. Radiology

- PAU/S
- Fundus examination
- ± CT brain
- Slit lamp.

Assess for the need of liver transplantation by the hepatologist.

IV. Treatment

1) Position: 20° + Insert → Ryle, urinary catheter
→ ± Central line

2) Fluids:

Amount: according to pt's hydration state

Aim: to maintain circulation, adequate intravenous volume & blood pressure.

Warning: avoid +ve balance (cerebral edema).

Type: * Glucose: Saline = 4 : 1 10-25% Glu ± K^+ maintenance

* Stop proteins till stabilization

3) Drugs:

- Vitamin K IV 2-10 mg daily.
- H_2 blockers: 2-4 mg/kg/day (8 hrs) or PPI: 1-2 mg/kg/D (24 hr).
- IV antibiotics

  + IV antifungal

  + IV antiviral e.g. acyclovir 20 mg/kg/ds(8hrs) in :

    a) if HSV PCR + ve

    b) for 1st 5 days in immunocompromised pts

    c) Infancy

    d) Cutaneous manifestation of herpes infection

- Intestinal antiseptics :

  Neomycin oral/Ryle: 50-100 mg/kg/day

  + Lactulose: 0.3 – 0.4 ml/kg 3 times/day → 2-3 motions/day

4. Management of cerebral edema:

I. Avoid fluid load, hypoglycemia, hypotension, hyper or hyponatremia avoid hepatotoxic and nephrotoxic drugs.

II. 1. Avoid sedation unless intubated

2. Give mannitol 0.5-1 gm/kg every 4-6 hrs.
3. No steroids as brain dehydrating measures.
4. Seizures should be treated with phenytoin and benzodiazepines with short half life as midazolam.

N.B.: Prophylactic phenytoin isn't recommended.

5. Maintain Bpr:

- Dopamine 5-20 mic/kg/min or noradrenaline 0.1-2 mic/kg/min
- ±Terlipressin. 20 µg/kg/ds every 4 hrs.
- ± Steroids hydrocortisone if resistant shock 25-50 mg/ds acc. to age

6. Blood and blood products transfusion:

- If blood transfusion is required, should be CMV –ve filtered irradiated blood.
- If bleeding:

1. Vit K IV.
2. FFP 10 : 15 ml/kg can be given every 6 hours
3. Cryo 1 unit/5 kg.
4. If non-responsive use factor VIIa 40 µg/kg over 2.5 mins.
5. PLT transfusion 6-10 units

   If PLT < 10.000/µl Or ≤ 50.000/ µl (for invasive procedure)
6. Tranexemic acid (dicynone) 10 mg/kg IV 6-8 hrs,

   Aminocaproic acid (cyclokapron) 400 mg/kg/day 6-8 hrs

If no bleeding: give FFP if → INR ≥ 7
→ Before invasive procedure

7) Hepatic ascites:

- Na^+ restriction → not exceeding 1 mEq/kg/D
  → Na^+ content of medication should be calculated
  → Avoid using high Na^+ content fluids except if Highly indicated e.g. (FFP, Ringer, Saline, $NaHco_3$)
- Fluid restriction 2/3 FM esp. if S.Na^+ < 120 – 125 mEq/L

Diuretic:

1. Spironoloctane 2 mg/kg/D ↑ every 4 days to reach max.
   Aim: 1) to reach –ve balance ≃ 10 ml/kg/day
   2)To avoid dehydration and renal impairment

If no response:

2. Loop diuretics with ratio 2.5 : 1 (aldactone : Lasix)
   If no response: for 1 wk→ manage as refractory ascites.
3. Theurapeutic paraceutesis:

- Volume 100 ml/kg or total
- Give 6-8 g/L albumin of removed ascites, to be give towards the end of tapping.

Nutritional support:

↑ Calories 20-30%,

Protein: 3-4 gm/kg/D (non-ecephalopathic),

:0.5-1 gm/kg/D (encephalopathic)

- Albumin infusion:

If S.albumin< 2.5 g/dl or with tapping , Dose : 1-2 gm/kg/ds

- If suspecting SBP: give 3rd generative cephalosporins till C &S.

8) Management of hematemesis of portal hypertension:

(1) Assessment of general condition, ABC + vital data bleeding (volume, rate).

(2) Immediate resuscitation:
   a) Ensure proper IV access.
   b) Airway protection with massive bleeding especially if comatosed.
   c) Fluid resuscitation in form of crystalloids 20 ml/kg over 20-30 min (then repeat if required) followed by
   d) PRBCs transfusion (don't exceed Hct around 30 or Hg 7-8 g%).

(3) Naso-gastric tube (safe & essential) for gastric washing using D 5%.
(4) PLT transfusion if less than 50.000/dL.
(5) Give konakion, FFP, Cryo ± (factor VIIa: if non responsive).
(6) H_2 blockers or PPI.
(7) Sandostatin continuous infusion:
   1-5 µg/kg/hr (max 25 µg/hr) and continued for 3-5 days
   A bolus 1 µg/kg may be given IV before infusion.
(8) Endoscopy: once the patient is stabilized → diagnostic
   →Therapeutic.

Acknowledgment:

This protocol was summarized from the protocol of Hepatology Clinic ASU, under supervision of Prof, Tawheda Yassin and hepatology clinic team.

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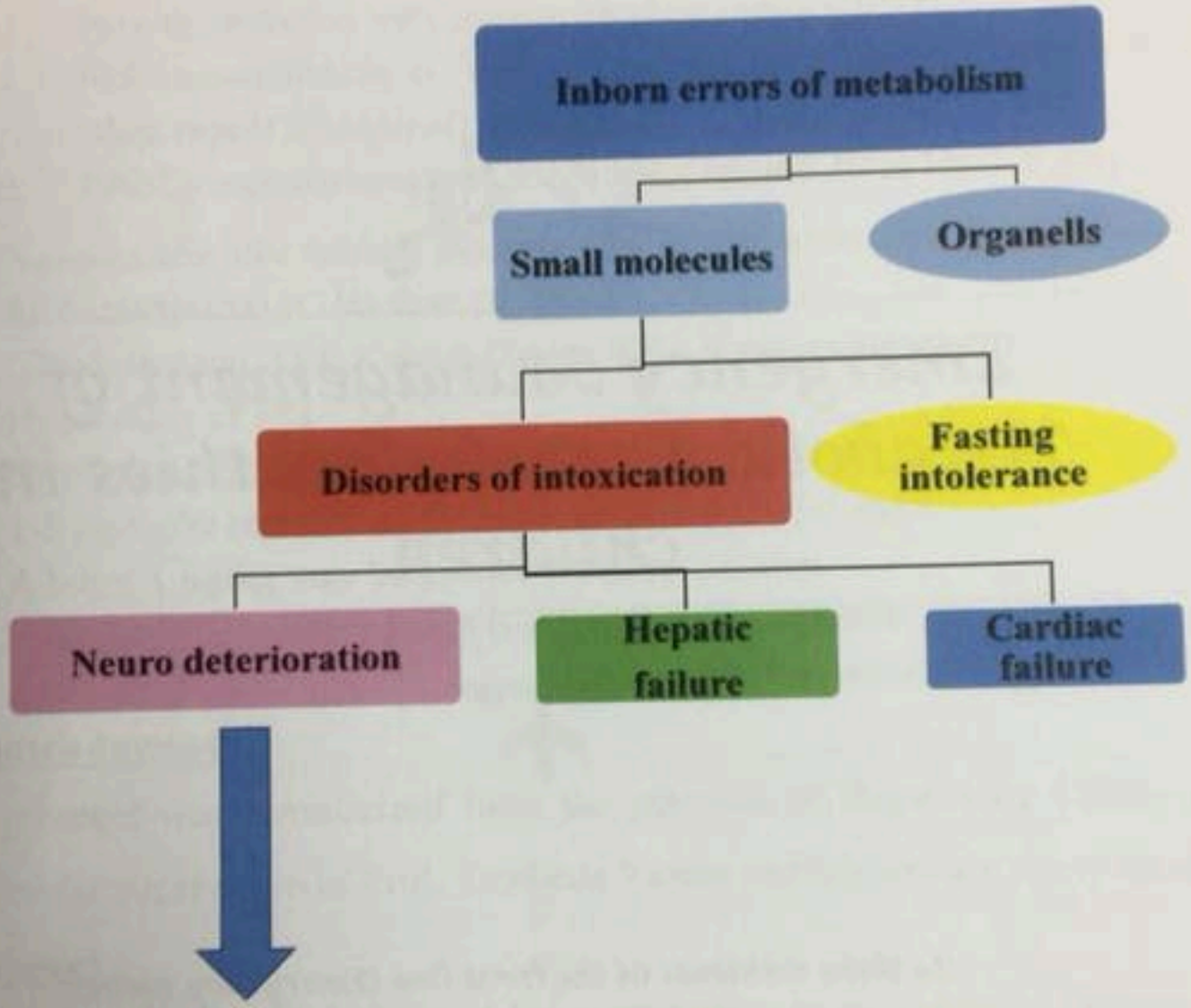
Emergency Management of Metabolic Encephalopathies in children

To those residents in the front-line (Emergency room)

By
Solaf M. Elsayed
Prof. of medical Genetics
Ain shams University

Therapeutic Classifications of Inborn Errors of Metabolism (IEM)



This booklet will include management of this part only

Intoxication is due to:

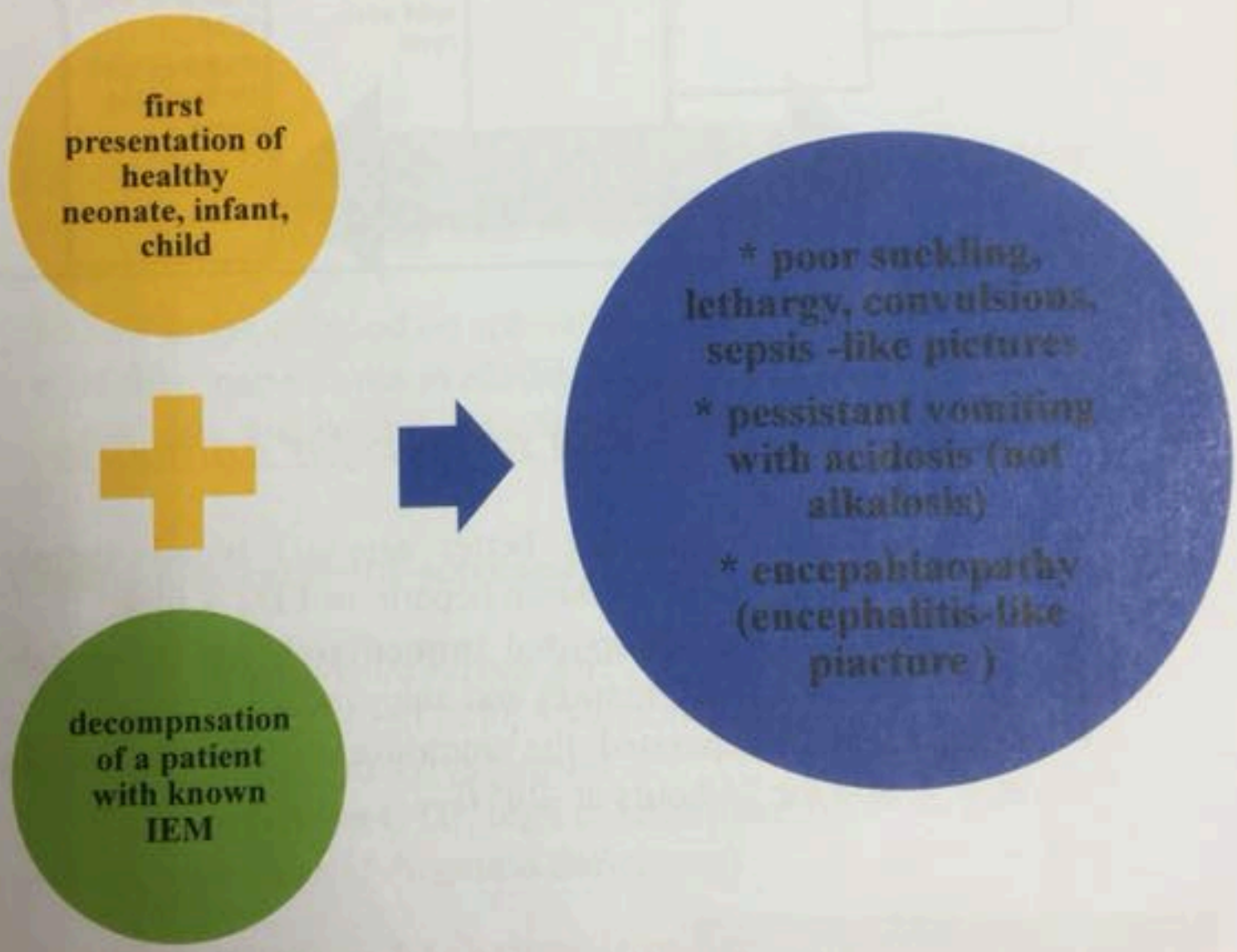
1. *Exogenous intake* of relatively larger amount of protein than the ability of body to metabolize.

2. *Endogenous* breakdown of protein during episodes of catabolism (stress): infection, surgery, fever.

With my Best wishes: Solaf M. Elsayed

Clinical scenarios

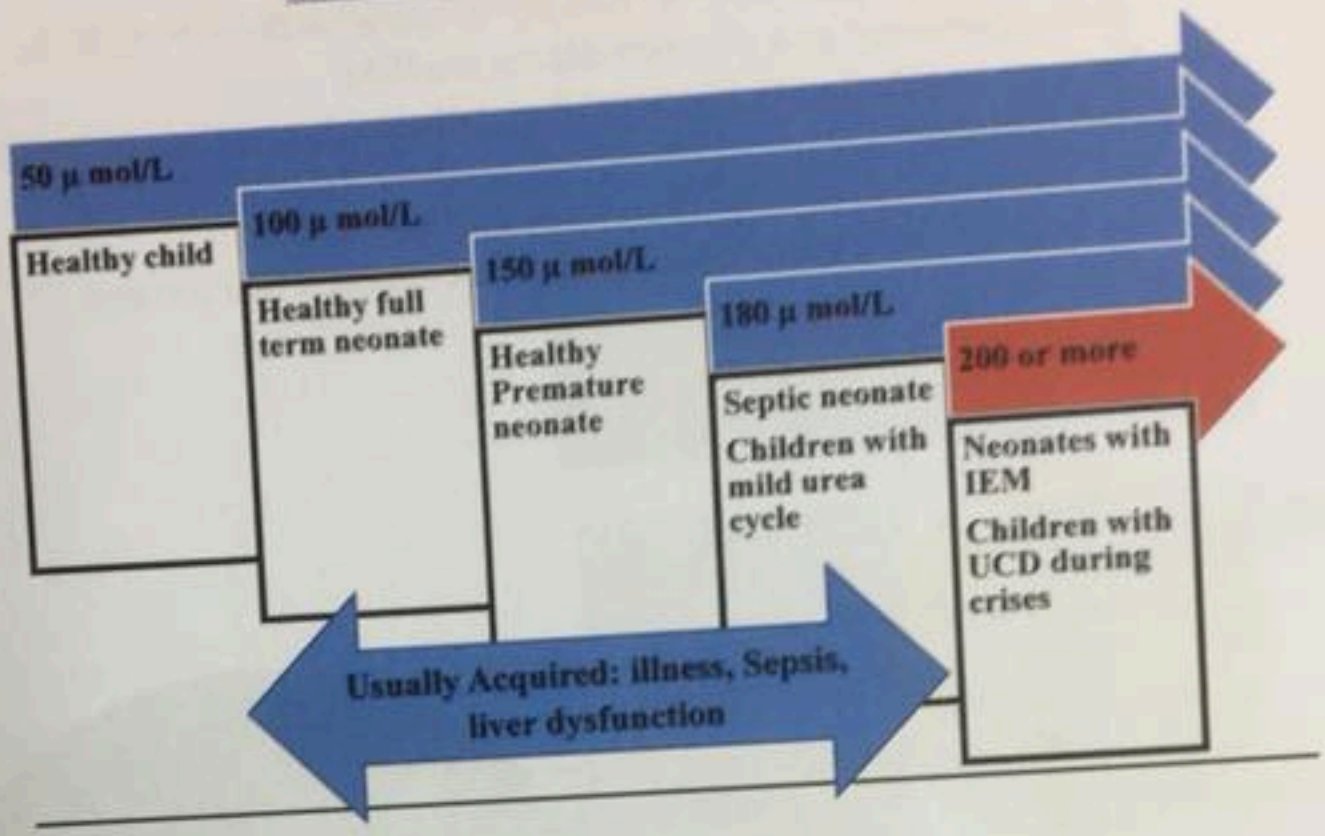
- Either first presentation of healthy neonate, infant or child or a decompensation of a patient with known IEM
- Neonate or infant with poor suckling, lethargy, convulsion or sepsis-like picture
- An infant/ child with persistent vomiting and acidosis
- An infant/child with encephalopathy (encephalitis like picture)



If there is any doubt at all, the child must be admitted, even for a short period of observation

With my Best wishes: Solaf M. Elsayed

Normal ammonia values



Precautions in taking samples for ammonia

- A free-flowing venous (or better arterial) blood sample should be collected on lithium heparin or EDTA tube.
- Sample should be transported **immediately** on ice to lab. Separated within 15 minutes and analyzed immediately.
- Once plasma is separated, the ammonia is stable for 4 hours at 4° C and for 24 hours at -20° C.

Pitfalls in taking samples for ammonia

- Difficult sampling and hemolysis can cause false increase.
- The ammonia of standing blood increase spontaneously due to: generation and release of ammonia from RBCs and to a lesser extent, from deamination of amino acids by enzymes in circulation

With my Best wishes: Solaf M. Elsayed

Pitfalls in measuring lactate

- Arterial samples are more reliable
- venous obstruction by tourniquet, crying, or breath holding may increase plasma lactate concentrations by two- to three folds!!!
- Serum lactate can also be increase in hypoxia, infections, convulsions, cardiac disease

Extended Metabolic Screen (EMS) using Tandem Mass Spectrometry (TMS)

- Few drops of blood on special filter paper
- If filter paper is not available, take one ml on heparin (green top) tube and keep it in Fridge (not freezer).

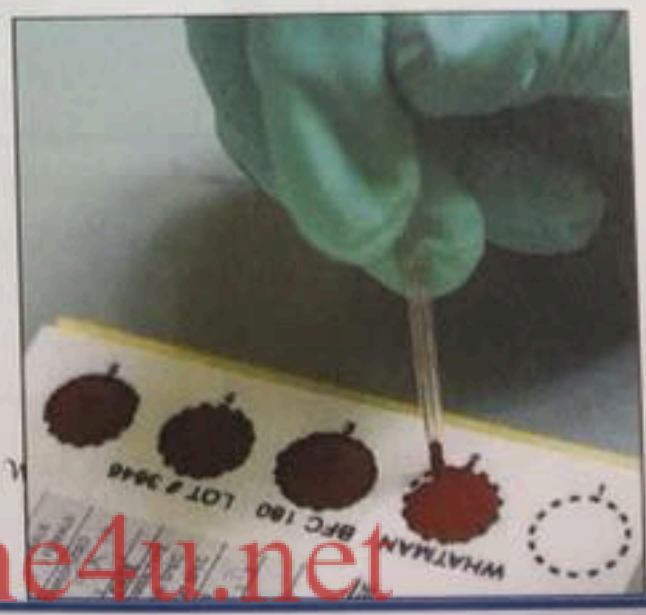
Compounds currently screened by EMS

1- Aminoacids profile screen for:

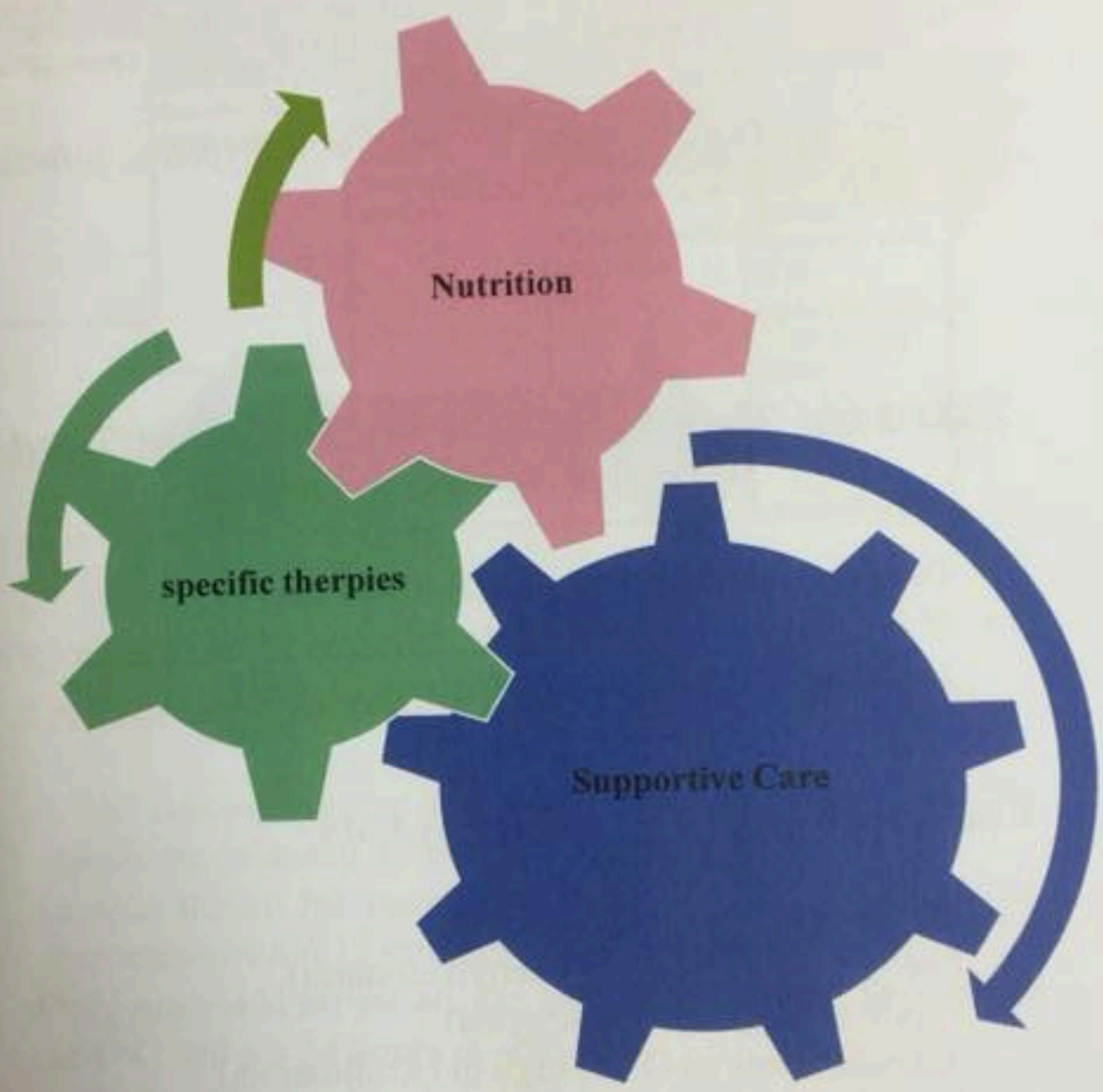
- Phenylalanine (high in Phenylketonuria)
- Tyrosine (high in Tyrosinemia)
- Citrullin (low in OTC, high in citrullinemia)
- Arginine (high in Arginase deficiency)

2- Acylcarnitine profile screen for:

- Fatty acid oxidation defects
- Organic acidemias



Pearls in management of IEM



REMEMBER

Aggressive treatment before the confirmation of a diagnosis may be lifesaving and may reduce the neurological squeals of some of these disorders

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1- **Supportive care:**

- Most patients will need rehydration, adequate calories, correction of acidosis, electrolytes, calcium, and phosphorus.
- Most patients have functional immunodeficiency which can result in persistent catabolism and therapeutic failure and so infections must be prevented and properly treated.

2- **Nutrition: Extremely important**

- Stop incriminated substance (protein). for not more than 24 hours
- Supply a good source of energy (IV glucose 10%)

3- Specific therapies:

- This is used for some disorders and includes substances that enable ammonia excretion (Na benzoate), carnitine, and vitamins (Cofactors).

Emergency Management of UNDIAGNOSED Inborn errors of metabolism

Aims:

1. Stop accumulation of toxic metabolites.
2. Prevention of catabolism (provide adequate calories) to prevent further catabolism
3. Enhance the excretion of toxic metabolites.
4. Co-factor therapy for specific disease and also empirically if diagnosis not established.
5. Symptomatic and Supportive care

Steps

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How to achieve Aims

1- Stop toxic metabolites

- Stop protein intake

2-Prevent further catabolism

- Provide adequate calories by glucose infusion (10%)/ pediament solution. (2 ml/kg over few minutes (then deficit and maintenance pediament solution).

- If hyperglycemia develop , add insulin (0.01-0.1 IU/kg/hr) to enhance anabolism. Monitor very closely and withdraw gradually with normalization of blood glucose

3- Enhance the secretion of toxic metabolites

- L-carnitine (IV or oral) 100 -200 mg/kg/day in 3-4 divided doses

4- Give all cofactors in undiagnosed patient

- Vitamin B1 and B6 : 100 mg/day each (Neurovit or neurobione)
- Vitamin B2 :100mg/day
- Vitamin B12 : Hydroxycobolamine (Depovit 1 mg/day)
- Biotine : Biotine fort: 10 -20 mg /day

5- Symptomatic and supportive care

- Correct dehydration (always needed)
- Correct acidosis if present
- Correct hyperammonemia if present
- Correct hypoglycemia if present
- Give antibiotic (always needed)
- Give anticonvulsants if needed

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A Useful check list

1- **Insert an IV access and a urine bag!**	

2- **Take samples**

A- **Basic laboratory investigations**

• Blood gases and pH, anion gap (venous)	
• Ammonia	
• Lactate	
• Serum glucose and urine ketones.	
• CBC, CRP	
• Electrolytes (Na, K, Ca, ph, Cl (if available))	
• ALT, AST	
• Creatinine, urea, uric acid	
• Coagulation studies	

B- Specific laboratory investigations:

Do not wait for the urine to start IV fluids

• Extended (expanded) metabolic screening (blood on filter paper or keep 1 cc blood on a heparinized tube)	
• Urinary organic acids including orotic acid (First voided urine) • keep it in the freezer if the lab is closed	

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3- Emergency treatment:

Fat should not be given till FAO defects have been excluded

Do not stop IV glucose of hyperglycemia develops. Start insulin 0.01-0.1 units /kg /h with close monitoring

1- **Stop intake** of all potentially toxic compounds (mostly **proteins**) for not more than 24 hours.	
2- **Give glucose infusion of a 10% solution** or pediament (2 ml/kg over few minutes. Then correct deficit and give maintenance solution	
3- **Give L carnitine** IV or oral at a dose of 200 mg/kg/day in three or four divided doses	
4- **Give vitamins** B1, B2, B6 (100 mg/day each or neurovit or neurobione). 5- Also, B12 hydoxycobolamine (Depovit) 1 mg /day IM 6- And biotine 10 mg/day (biotine fort) oral or IV	
7- Symptomatic and supportive care: • **Correction of dehydration** • **correction of hyperammonemia** • **correction of metabolic acidosis** • **Treatment of convulsions** • **Give antibiotics**	

- **Do not stop IV glucose of hyperglycemia develops.**
- **Start insulin at a dose of 0.01- 0.1 units /kg /h with close monitoring**

Treatment of hyperammonemia

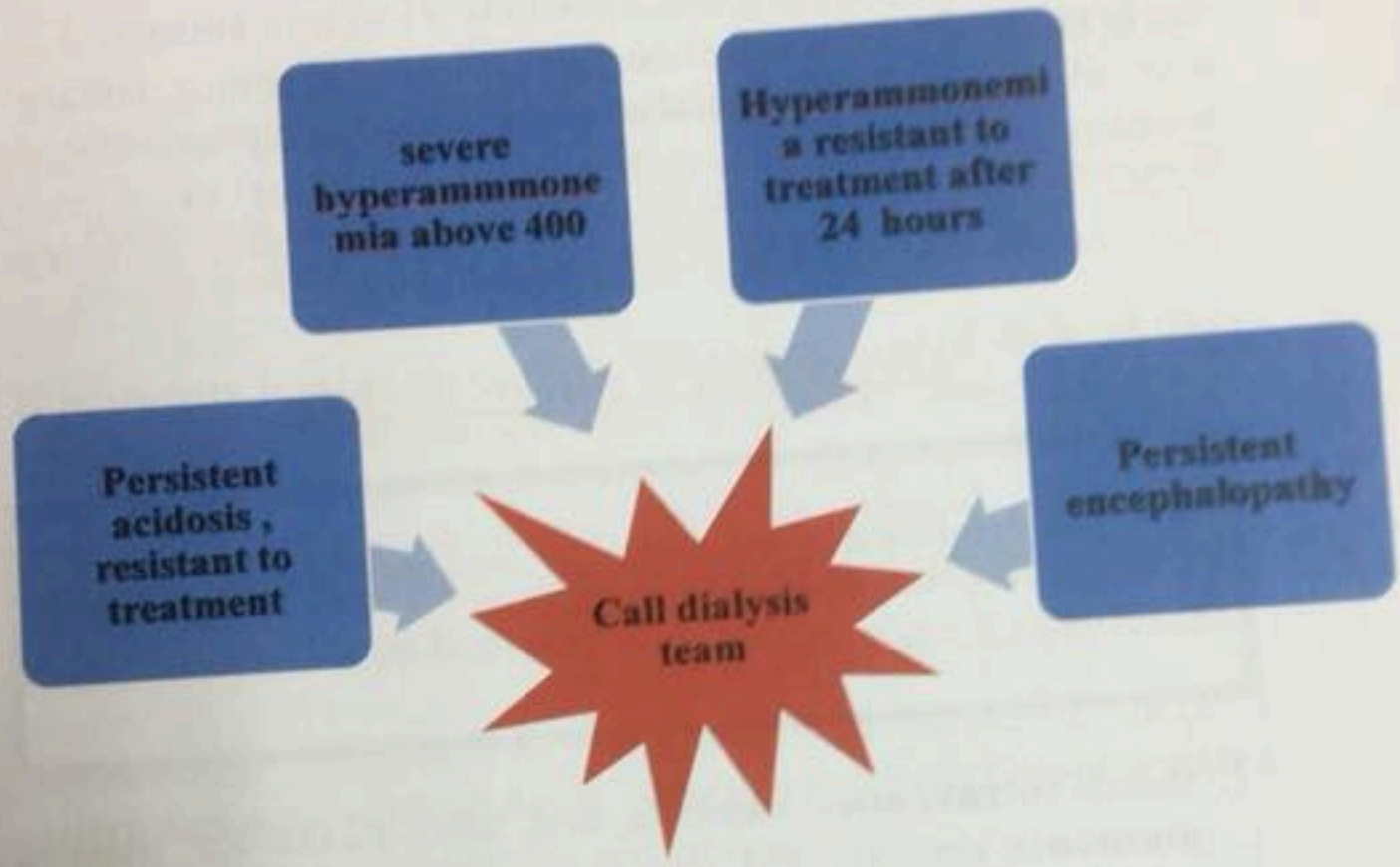
- You have already stopped protein intake
- Give Sodium benzoate or sodium phenylacetate 250 mg / Kg as a primary infusion in a 90 minutes period. Then 250 -500 mg/ Kg/day as a maintenance.
- You can add lactulose and neomycin/flagyl
- If ammonia level is > 400 u mol/ L or if its level does not decrease with conservative treatment in 24 hrs, peritoneal dialysis should be started.
- Entral nutrition (with restrictions) should be started ASAP by continuous entral slow drip feeding via nasogastric tube with minimal amount of protein (0.25 gm / Kg / day) during the first 24 hours of therapy.

Treatment of metabolic acidosis

1- **Correct dehydration**
2- if acidosis persists after correction of dehydration, give sodium bicarbonate if **the pH <7.2** or the **pH is deteriorating rapidly** or the **base deficit is greater than 10 mmol/l.**
3- Give a half correction [0.6 x body weight x base deficit] with sodium bicarbonate **over at least 30 minutes**. And reche
4- Repeat **once** if necessary and keep an eye on plasma **sodium** concentrations. **Aggressive therapy with repeated boluses of IV bicarbonate may induce hypernatraemia, cerebral oedema, and even cerebral haemorrhage.**
5- If no response, and the patient is well hydrated, have no cardiomyopathy or pancreatitis, **CALL for peritoneal dialysis and ventilator support**
6-

Severe acidosis (pH <7.2 or base deficit > 10 mmol/l) **is potentially very dangerous.** Patients may have a respiratory (or cardiac) arrest and are usually difficult to resuscitate. **Always** consider elective assisted ventilation

When to call the dialysis team ???



Impending death and Post mortem samples

- Urine, frozen: organic acids
- Frozen heparinized plasma (Do not use EDTA): aa, carnitine/acylcarnitine profile
- A small snip of skin obtained using sterile technique and stored in tissue culture medium, or sterile saline.
- A liver biopsy (Additional tissue should be preserved for electron microscopy.)

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Management of specific diseases

Urea Cycle defect due to OTC deficiency

Decompensation is often triggered by metabolic stress: febrile illness, fasting and any protein loading but sometimes there is no apparent cause.

Early signs of decompensation may be subtle: vomiting, lethargy, loss of appetite or exacerbation of pre-exiting neurological problems (irritability, fits, etc) or just does not feel ok. At early stages the ammonia is not so increased because glutamine accumulates first and leads to cerebral oedema.

Always listen to parents carefully.

Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or is behaving oddly.
Do not delay if you are uncertain.

1. Insert **intravenous cannula** and send blood for **plasma ammonia** urgently and also for urea, electrolytes, glucose, CBC, blood culture.

2. **Stop intake of protein**

3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids. If hyperglycemia develops, start insulin as indicated before.

4. Give loading dose of **sodium benzoate** 250 mg/kg (added to glucose over 1-2 hours) then maintenance sodium benzoate 250-500 mg/kg/day.

5. **Arginine** (Note: some parents carry supplies of these): 200-600 mg/kg and maintenance of 100-170 mg/kg/day (some patients may need up to 400-700mg/kg/day)

6. Prevent constipation by giving lactulose

7. **Carnitine** oral or IV at dose of 100 mg/kg/day

8. Give antibiotic and properly treat infection.

9. Potassium should be added once urine flow is normal and the plasma potassium concentration is known.

If ammonia level is more than 400 u mol/ L or if its level does not decrease with conservative treatment after 24 hours, continuous venous hemodialysis or haemoinfiltration or haemodiafiltration, peritoneal dialysis should be started depending on the local availability of the method and the experience of the medical staff.

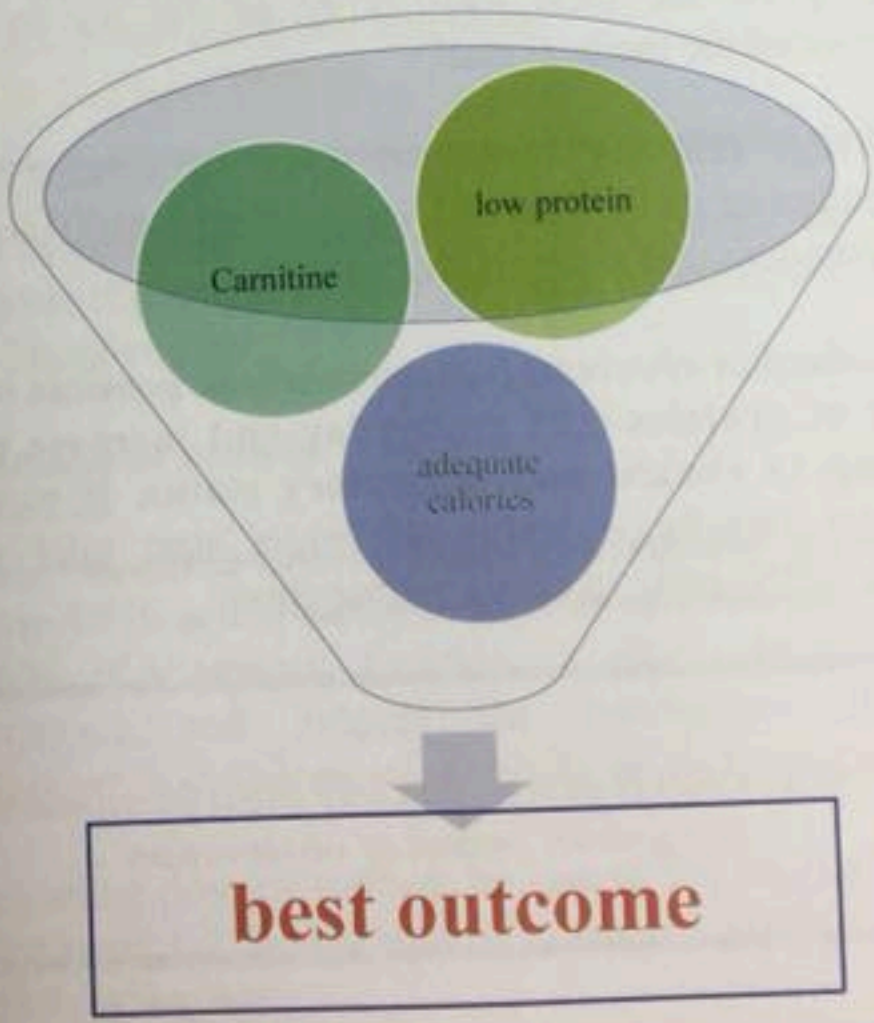
Monitoring: reassess every 4-6 hours or earlier if there is deterioration of clinical status. Assess using both Glasgow coma scale, ammonia, glucose and electrolytes

***Re-introduction of enteral feeds*: as early as possible with small amount of proteins 0.25 gm/kg/day and increase gradually according to clinical and laboratory status.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

If there is any doubt at all, the child must be admitted, even for a short period of observation

Pearls in Emergency Management of Organic acids disorders

For many organic acid disorders, early diagnosis and treatment can significantly change the outcome of the patient. Improved outcome is noted in most cases when the infant is provided ***a low-protein diet and carnitine supplementation****. For some organic acid disorders,* ***additional dietary supplements and/or vitamins are recommended****. Aggressive treatment during metabolic crises, including glucose administration, is recommended.*



Methylmalonic acidemia (MMA)

MMA is caused by a deficiency of methylmalonyl CoA mutase, an enzyme on the catabolic pathway of protein metabolism (methionine, threonine, valine and isoleucine) and cholesterol side chains, odd chain fatty acids and free propionate from the gut. **The co-factor for the enzyme is a derivative of vitamin B_{12} (hydroxocobalamin).**

Decompensation is often triggered by **metabolic stress** such as febrile illness, particularly diarrhoea or vomiting, fasting or constipation, but **an obvious precipitant cause is not always apparent.** Early signs of decompensation may be subtle: lethargy, decreased appetite, irritability or just "does not look ok". Vomiting is common and should always be taken seriously.

Please always listen to parents carefully

- **Dehydration** is a common problem because of the renal disease and polyuria.
- **Emergency treatment should be meticulous as there is a high risk of serious complications like encephalopathy, stroke like episode, metabolic acidosis, pancreatitis and cardiomyopathy.**
- **Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain.**

In MMA, the maintenance fluid is calculated as follows (because of increased fluids requirements: **120ml/kg for 1st 10 kg then 60 ml/kg for next 10 then 25ml/kg).**

1. Insert **intravenous cannula** and send blood for **plasma ammonia, pH, blood gases and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine, amylase. calcium, phosphorus and alkaline phosphatase.**

2. **Stop protein intake (for not more than 48 hours)**

3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg over few minutes until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids. **Insulin may be added as indicated before**

4. **Give L- Carnitine** oral or IV at dose of 200 mg/kg/day in 3-4 doses. (some references advise a loading dose of 100 mg/kg over 30 minutes followed by a continuous infusion of 4mg/kg/hour as a maintenance)

5. **Correct metabolic acidosis** as described before.

6. **Correct hyperammonemia as described before.**

7. Give **Metronidazole** 7.5 mg/kg per dose 8 hourly

8. If the patient is vitamin B_{12} responsive or B_{12} status is not known, give **hydroxocobalamin 1 mg intramuscularly**

9. Treat any **infection with proper antibiotics**

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10. Treat **constipation** (which increases propionate absorption from the gut).

11. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

** ***Pancreatitis*** is suspected if there is abdominal pain, shock out of proportion of other symptoms or hypocalcemia. Check plasma lipase and amylase and arrange for abdominal ultrasound. Plasma lipase and amylase activity should be repeated as these **may not be raised, particularly at an early stage.**

****Cardiomyopathy*** may develop for no reason at any time. If you suspect cardiomyopathy arrange for Echocardiography and call for cardiologist.

Monitoring: reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: clinical assessment with Glasgow coma score, blood pH and gases, ammonia, glucose, lactate, urea and electrolytes, full blood count, calcium, phosphate, ALP and amylase/lipase if pancreatitis a possibility.

Enteral feeds with some protein **should be introduced as early as possible, as this allows a much higher energy intake and reduces the risk of malnutrition.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

Medicines to be avoided - Sodium Valproate

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Propionic acidemia

It is one of the protein IEM caused by a deficiency on propionyl CoA carboxylase, an enzyme on the catabolic pathway of aminoacids (isoleucine, valine, threonine and methionine) as well as cholesterol side chains, odd chain fatty acids and free propionate from the gut.

Decompensation is often triggered by metabolic stress such as febrile illness, particularly diarrhoea or vomiting, fasting, or constipation. Decompensation may be manifested by lethargy, refusal of eating, irritability or just 'not right'.

- **Please, always listen to parents carefully.**

- **Emergency treatment should be meticulous as there is a high risk of serious complications like encephalopathy, stroke like episode, metabolic acidosis, pancreatitis and cardiomyopathy.**

- **Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain.**

1. Insert **intravenous cannula** and send blood for **plasma ammonia, pH and blood gases and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine, amylase. calcium, phosphorus and alkaline phosphatase.**

2. **Stop protein (for not more than 48 hours).**

3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids

4. **Correct metabolic acidosis** as described before

5. **Correct hyperammonemia** as described before

6. **Give Carnitine** oral or IV at dose of 100 – 200 mg/kg/day

7. Give **Metronidazole** 7.5 mg/kg per dose 8 hourly

8. Treat any **infection with proper antibiotics**

9. Treat **constipation** (which increases propionate absorption from the gut). Do **not** use lactulose as this can be fermented to propionate by gut bacteria)

10. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known

** ***Pancreatitis*** is suspected if there is abdominal pain, shock out of proportion of other symptoms or hypocalcemia. Check plasma lipase and amylase and arrange for abdominalultrasound. Plasma lipase and amylase activity should be repeated as these **may not be raised, particularly at an early stage.**

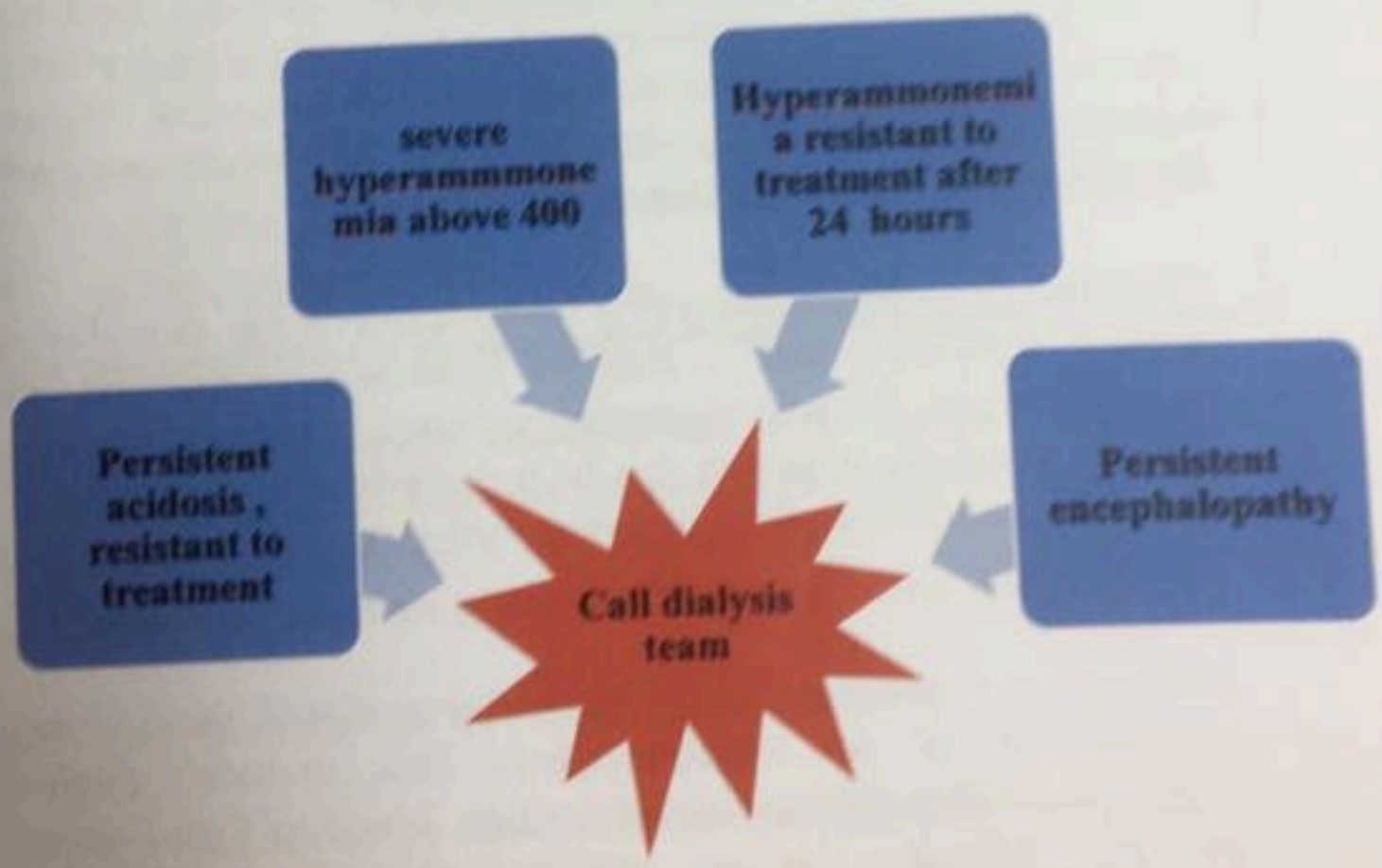
****Cardiomyopathy*** may develop for no reason at any time. If you suspect cardiomyopathy arrange for Echocardiography and call for cardiologist. Cardiac arrhythmias, notably long Q-T, are an important complication that may be responsible for sudden death. These may vary from time to time so all sick patients should be on a monitor.

Monitoring: reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: clinical assessment with Glasgow coma score, blood pH and gases, ammonia, glucose , lactate , urea and electrolytes, full blood count, calcium, phosphate, ALP and amylase/lipase if pancreatitis a possibility.

Enteral feeds with some protein **should be introduced as early as possible, as this allows a much higher energy intake and reduces the risk of malnutrition.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

Medicines to be avoided - Sodium Valproate; Lactulose.

If there is any doubt at all, the child must be admitted, even if only necessary for a short period of observation.



Isovaleric acidemia

Isovaleric acidaemia is caused by a deficiency of isovaleryl CoA dehydrogenase, **an enzyme on the catabolic pathway of leucine**. Treatment is aimed at reducing production of isovaleric and increasing its removal. **The patients are treated with a low protein diet, glycine and carnitine**

Decompensation is often triggered by metabolic stress such as febrile illness, particularly diarrhoea or vomiting, fasting, or constipation. Decompensation may be manifested by lethargy, refusal of eating, irritability or just 'not ok'.

Please, always listen to parents carefully.

Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain. There is high incidence of pancreatitis

1. Insert **intravenous cannula** and send blood for **plasma ammonia, pH and blood gases and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine and amylase, calcium, phosphorus, alkaline phosphatase**

2. **Stop protein (for not more than 48 hours).**

3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids

4. **Correct metabolic acidosis** as described before

5. **Correct hyperammonemia** as described before

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6. **Give Carnitine** oral or IV at dose of 100 – 200 mg/kg/day

7. Give **Glycine** via nasogastric tube at a dose of 300 mg/kg per day.

8. Treat any **infection with proper antibiotics**

9. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known

** ***Pancreatitis*** is suspected if there is abdominal pain, shock out of proportion of other symptoms or hypocalcemia. Check plasma lipase and amylase and arrange for abdominal ultrasound. Plasma lipase and amylase activity should be repeated as these **may not be raised, particularly at an early stage.**

Monitoring: reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: clinical assessment with Glasgow coma score, blood pH and gases, ammonia, glucose, lactate , urea and electrolytes, full blood count, calcium, phosphate, ALP and amylase/lipase if pancreatitis a possibility.

Enteral feeds with some protein **should be introduced as early as possible, as this allows a much higher energy intake and reduces the risk of malnutrition.** If enteral feeds cannot be introduced within 48 hours start total parenteral nutrition (TPN) early to avoid malnutrition.

If there is any doubt at all, the child must be admitted, even if only necessary for a short period of observation.

Maple syrup Urine disease (MSUD)

MSUD is disorder affecting the breakdown of branched chain amino acids (BCAA: Leucine, Isoleucine & Valine). Encephalopathy in decompensated patients is the result of accumulation of the BCAA (particularly leucine), which are toxic at high concentrations. **There may be NO hypoglycemia, hyperammonaemia or acidosis.**

Decompensation: often triggered by metabolic stress such as febrile illness, particularly gastroenteritis or fasting but **an obvious cause is not always apparent.**

Early signs: lethargy, irritability or just 'not right'. **vomiting is common and should always be taken seriously.**

Please Always Listen to parents carefully

Treatment aims: at a point you may need individual aminoacids

- *Inhibit protein catabolism and promoting anabolism* by providing **high calorie intake** combined with the **child's usual MSUD amino acid formula.**
- *Lower BCAA levels* by **stopping or restricting 'natural protein.**
- Ensure *a balance is maintained between leucine, isoleucine and valine* during decompensation giving **supplements of individual aminoacids.**

1. Insert **intravenous cannula** and send blood for **plasma aminoacids or EMS (whatever available) , pH and blood gases, CBC and glucose urgently. Please ask also for CBC, lactate, electrolytes, creatinine and amylase.**

2. **Stop protein intake**

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3. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids **Hyperglycaemia can be a problem. If hyperglycemia developed start an insulin as indicated before.**

4. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

5. Intra-lipid may be added 2g/kg/d (0.4ml/kg/hour of 20% solution).

6. Treat any infection properly

7. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known

Monitoring: Reassess after 4-6 hours or earlier if there is any deterioration or no improvement call for peritoneal dialysis (although less efficient than hemodialysis).
Re-introduction of enteral feeds: enteral feeds should be used as early as possible to promote anabolism and protein synthesis.

The BCAA free aminoacid mixture should be given as tolerated and natural protein introduced adjusted according to the plasma BCAA concentrations. The branch chain aminoacid free aminoacid mixture should be added starting with a low dose 0.5 g /kg/d. This should be increased as quickly possible to 2 g/kg/d.

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Fatty Acid Oxidation defects (FAO)

Please Always listen to parents carefully

- **Hypoglycaemia only occurs at a relatively late stage (or very late) so Do not delay treatment just because the blood glucose is not low.**
- **The aim should always be to intervene whilst the blood glucose is normal.**

- ***Decompensation*** is often triggered by metabolic stress such as febrile illness, infections, fasting and particularly vomiting and diarrhea can lead to serious illness with encephalopathy and hypoglycaemia. The early signs of decompensation may be subtle **(lethargy or 'floppiness)**.

The major complications are **encephalopathy, cardiomyopathy, hypoglycaemia and rhabdomyolysis.**

Treatment aims:

1. To restore carnitine concentrations
2. Reduce mobilization of fat by providing ample glucose - enteral or intravenously.

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Start this treatment if the patient is obviously unwell, vomiting, drowsy, uncooperative or acidotic. Do not delay if you are uncertain.

1. Insert **intravenous cannula** and send blood pH and blood gases Glucose (laboratory and bedside strip) CBC, creatinine, electrolytes.

2. **Provide adequate calorie, fluids and electrolytes IV: Give Glucose 10%** at 2-5 ml/kg/h. until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids

3. **Give Carnitine** IV at dose of 100-200 mg/kg/day, oral if IV carnitine is not available

4. Treat any **infection with proper antibiotics**

5. Treat metabolic acidosis if present

Monitoring: Reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: Clinical assessment with Glasgow coma score, Blood pH and gases , Glucose , Urea and electrolytes.

Restart oral feeds as soon as possible; once the child is has stopped vomiting.

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Rhabdomyolysis, myoglobulinuria

- The early signs may be subtle **(weakness, lethargy or 'floppiness)**

Please Always listen to parents carefully

Emergency treatment should be meticulous as there is a high risk of serious complications including:

- Leakage of myoglobin into the systemic circulation, with a risk of **renal vasoconstriction and acute renal failure**
- The leakage of potassium into the systemic circulation, with potentially life-threatening **acute hyperkalaemia**
- **hyperuricaemia** due to release of purines from disintegrating cell nuclei
- **Hyperphosphataemia** may be due to efflux from damaged muscle cells with potential metastatic calcification and **hypocalciemia**
- **Metabolic acidosis** and aciduria

Start treatment immediately with the first sign of weakness and lethargy. **Do not delay if you are uncertain. DO NOT wait till you see the colour of urine.**

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1. Insert **intravenous cannula** and **send samples for** CPK, urine myoglobin, potassium, calcium and phosphorus, acid-base status, uric acid, urea and creatinine measurements.

2. Maintenance **of adequate preload and urine output**

3. Maintenance **fluid at 2 – 3 x normal requirements**.

4. **Alkalinisation of urine,** (sodium bicarbonate 1 – 3 mmol/kg/day (IV or orally depending on the clinical status of the patient), given as doses every 4 – 8 hrs) to protect against myoglobin-induced renal failure. **Aim to keep urinary pH above 6.5.** If metabolic alkalosis develops (pH > 7.45) there is a theoretical risk of enhancing metastatic calcification

5. Haemodialysis may be necessary for acute renal failure.

6. Treat any **infection with proper antibiotics**

Monitoring: Reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: Clinical assessment , urine output, Blood and urine pH Urea, creatinine, uric acid, ca, phosphorus, K and **CPK**

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.

Glutaric aciduria type I (GA type I)

GA type I is a rare inborn error of protein metabolism due to glutaryl-CoA dehydrogenase deficiency which is involved in processing lysine, hydroxylysine, and tryptophan metabolism. Excessive levels of these amino acids and their intermediate breakdown products cause damage to the brain, particularly the basal ganglia.

The **characteristic neurological sequela** is secondary dystonia, superimposed on axial hypotonia.

Emergency treatment should start without delay and should be performed aggressively during febrile illness Gastroenteritis, poor food intake, surgery

1. Insert **intravenous cannula** and send blood for **pH and blood gases, CBC, electrolytes and blood culture.**

2. Stop intake of natural proteins (not more than 24 hours) and then gradually introduce it. Prolongation of inadequately low protein intake increases the risk of protein catabolism.

3. Give high dose IV glucose (2 ml/kg of 10% glucose or pediament) until the maintenance solution is ready (Pediament): Quickly calculate the deficit and maintenance and prepare the intravenous fluids. If hyperglycemia develop add insulin as previously indicated.

4. **Double the dose of L-carnitine** to 200 mg/kg/day

5. Correct the metabolic decompensation as metabolic acidosis, electrolytes, and ammonia

6. Increase caloric intake by frequent carbohydrate feeds especially liquids if tolerated. If lysine free aminoacid mixture available and can be tolerated orally or via naso-gastric tube start with 0.5 g/kg/d but for as short a period as possible. **Do not delay giving other treatment if the mixture is not immediately available.**

7. If body temperature raises above 38.5 °C, antipyretics, such as ibuprofen or paracetamol (each 10-15 mg/kg per single dose, 3-4 doses daily, maximum daily dose 60 mg/kg body weight) should be administered.

8. Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

Monitoring: Reassess after 4-6 hours (or earlier if there is any deterioration or no improvement). This include: Clinical assessment with Glasgow coma score, Blood pH and gases , Glucose , Urea and electrolytes.

Re-introduction of enteral feeds: enteral feeds should be used as early as possible to promote anabolism and protein synthesis

Valpoaric acid and Vigabrtin are CONTRAINDICATED

If there is any doubt at all, the child must be admitted, even if only for a short period of observation.